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The Archives of Internal Medicine

VOL. XIX. MAY, 1917.—IN TWO PARTS. PART II. No. 5

CLINICAL CALORIMETRY

NINETEENTH PAPER *

THE BASAL METABOLISM OF OLD MEN *

JOSEPH C. AUB, M.D., AND EUGENE F. DU BOIS, M.D.
WITH THE TECHNICAL ASSISTANCE OF G. F. SODERSTROM
NEW YORK

The question of the basal metabolism at various ages has been discussed in Paper 12 of this series, and the references to the literature have already been published. It was apparent that our knowledge of the energy exchanges in old age depended almost entirely on the careful work of Magnus-Levy and Falk[1] who studied five old men and seven old women. These results were used by us in drawing the curves which indicated the average level of metabolism at various ages, but it was apparent that after the age of 43 the points on the chart were scanty. This present work is an attempt to fill in the gap.

An effort was made to find men 90 to 100 years old, but it was impossible to obtain suitable subjects. The age limits were then reduced to between 75 and 85 years, and, after much labor, six men were obtained who fulfilled the requirements. They were either inmates of the New York City Home for Aged and Infirm on Blackwell's Island, or men from other institutions about to be transferred to this home. They were all in good condition and fairly well nourished, though on plain and somewhat scanty diets. Considering their ages, they were in good health, though most of them suffered from arteriosclerosis, chronic interstitial nephritis and emphysema, which "normally" accompany advanced years. They were about as active as most persons of their time of life, none of them being engaged in regular work.

The men were selected by one of the writers from the somewhat limited number over 75 years of age who were in the City Home or Municipal Lodging House. Only those in fair health, with clear and apparently reliable histories as to their ages, were chosen, and an effort

* Submitted for publication Dec. 19, 1916.

* Clinical Calorimetry, Eighteenth Paper, The Number of Places of Significant Figures in the Data of Metabolism Experiments, by Gephart, Du Bois and Lusk was published in the Journal of Biological Chemistry, 1916, **27,** 217.

* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division, Bellevue Hospital.

1. Magnus-Levy and Falk: Der Lungengaswechsel des Menschen in verschiedenen Alterstufen, Arch. Anat. u. Physiol., 1899, Suppl., p. 315.

was made to pick out men who would cooperate in the experimental procedure. Most of them were delighted with the change of food and scene when they were taken from the almshouse to the metabolism ward. All the experiments were made in the morning, the men being placed in the calorimeter with no breakfast except a cup of "caffein-free" coffee. The old men were about as quiet as the younger controls, with the exception of one whose test had to be repeated.

CASE HISTORIES

CASE 1.—*History.*—Andrew O'C., 77 years old, formerly a car driver, now an inmate of City Home. As a young man he served in the army at the outbreak of the Civil War. He says that he has never been sick, except two years ago, when he was in the hospital for two months with fever. The hair in the axillae has always been scant and he has never had any hair on his thorax. During most of his life he drank about a pint of whisky a day but has had none for six months. He has had no libido for seven or eight years. Recently he has been spending his winters in the City Home and his summers at work. He feels perfectly well and gives no symptoms except frequency of urination at night.

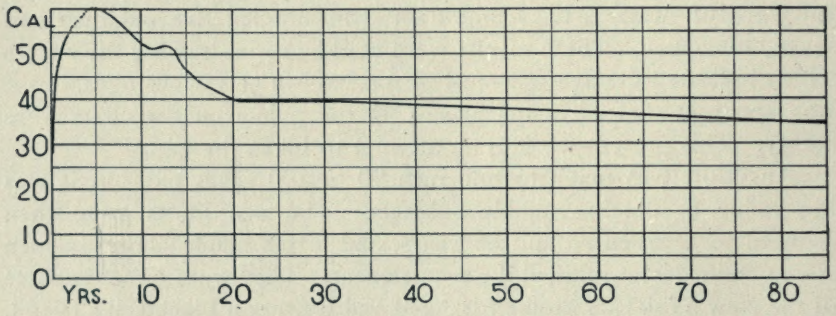


Fig. 1.—Curve showing the level of metabolism at different ages. Results are expressed in terms of calories per hour per square meter of surface area (Linear and Height-Weight Formulas). In accordance with the findings in the present series, the line is somewhat higher in old age than in the curves published in previous papers.

Physical Examination.—A well nourished man, with white hair and slightly wrinkled skin, who looks about 65 years old. No arcus senilis. Heart sounds are of good quality, with an occasional premature systole. There is a faint blowing systolic murmur at the apex. Blood pressure: 235 mm. systolic; 100 mm. diastolic. The pubic hair is scant and of feminine type. Genitalia normal.

The man was of active disposition and spent most of his time walking about the ward. He was the least senile of the group.

CASE 2.—*History.*—Henry L., 78 years old, formerly a baker, now an inmate of City Home. Six years ago he broke his leg and was in the hospital five months. He passes urine twice at night. He has used alcohol sparingly, but has taken a great deal of snuff.

Physical Examination.—Well nourished, skin wrinkled, looks his full age. There is a slight tremor of the hands. Thorax deep, breath sounds emphysematous, with fine râles at the bases. The left border of the heart percusses

13 cm from the median line. There are a few premature systoles; no murmurs. The radial walls are not palpable. Blood pressure: 155 mm. systolic; 80 mm. diastolic.

His disposition was quiet and he spent most of his time in the hospital sitting in a chair. The first time he was in the calorimeter, March 13, he did not understand the instructions and was very restless, taking snuff, coughing, sneezing and moving about. The second time he was in the calorimeter, March 18, he was quiet and the observation was satisfactory.

CASE 3.—*History.*—Charles H., 79 years old, formerly a cigar maker, now in City Home. Ten brothers and sisters lived to be over 70 years of age. Two years ago he had pneumonia. He passes urine two or three times at night. He has been a moderate drinker of beer and a heavy smoker. No libido for the past five years. He feels perfectly well except for a slight cough in the morning.

Physical Examination.—Rather thin, skin flabby and much wrinkled; well preserved for his age. Thorax deep; breath sounds emphysematous. Left border of cardiac dulness 15 cm. from median line. Blood pressure: 210 mm. systolic; 100 mm. diastolic. Urine contains trace of albumin.

His disposition was active and restless and he spent most of his time standing about the ward or working.

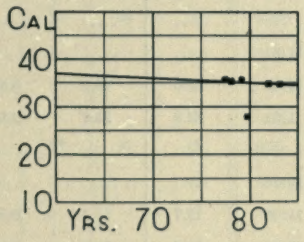


Fig. 2.—Part of Figure 1 with dots representing the findings in the old men of this series.

CASE 4.—*History.*—Charles W., 80 years old, formerly a waiter, for the last year and a half an inmate of City Home. Two years ago his arm was injured in an accident. He was formerly very alcoholic. Fifty-five years ago he had lues. No libido for seven years.

Physical Examination.—Well nourished, skin wrinkled, left border of cardiac dulness 14 cm. to left of median line. At the apex there is a faint systolic murmur. Blood pressure: 180 mm. systolic; 80 mm. diastolic. Breath sounds are emphysematous, with coarse râles at the bases. The urine is normal. Wassermann reaction negative.

This was the most senile of the group. All day long he sat motionless in his chair, taking but little interest in his surroundings.

CASE 5.—*History.*—William C., 83 years old, formerly a newspaper writer, now waiting to be admitted to the City Home. He has had no alcohol for the last forty years, but has smoked excessively. His health has always been good. One week ago he developed a slight cough.

Physical Examination.—Well nourished, skin wrinkled, hair white. Heart normal except for occasional premature systoles. The breath sounds are emphysematous. His disposition is cheerful and he is fairly active. The urine contained 49 gm. glucose on a carbohydrate intake of 190 gm. daily. He had no acidosis.

CASE 6.—*History.*—John B., 83 years old, formerly a storekeeper, now waiting in Bellevue Hospital until he can find a place in a home for the aged.

TABLE 1.—Old Men. Data of-

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period.	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 1.....	Prelim.	10:35	.....	.....	.....	.....	.....	.....	.....
(Andrew O'C.) 5/8/16	1	11:35	22.3	20.0	0.82	34.6	0.562	66.3	78.0
69.7 Kg. 1.87 Sq. M.	2	12:35	22.5	20.0	0.82	34.6	0.562	66.3	78.0
	Aver.	.....	.....	.....	.....	.....	.....	66.6	.....
Case 2 (Henry L.) 3/13/16	Prelim.	11:43	.....	.....	.....	.....	.....	.....	.....
67.9 Kg. 1.85 Sq. M.	1	12:43	24.6	22.2	0.81	31.6	0.2885	74.2	75.3
	2	1:43	25.1	24.2	0.76	34.6	0.2885	79.8	79.9
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Henry L.	Prelim.	11:31	.....	.....	.....	.....	.....	.....	.....
3/18/16 68.9 Kg. 1.85 Sq. M.	1	12:31	22.0	18.0	0.89	19.9	0.291	61.8	63.9
	2	1:31	23.8	20.7	0.84	25.0	0.291	69.5	72.7
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Case 3 (Chas. H.).	.....	10:26	.....	.....	.....	.....	.....	.....	.....
5/3/16 52.9 Kg. 1.66 Sq. M.	1	11:16	15.7	14.1	0.81	22.4	0.238	47.2	46.0
	2	12:26	23.4	21.2	0.80	32.1	0.238	70.8	70.9
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Case 4 (Chas. W.)	Prelim.	10:31	.....	.....	.....	.....	.....	.....	.....
5/4/16 69.1 Kg. 1.82 Sq. M.	1	11:31	17.3	15.4	0.82	27.5	0.228	51.5	60.4
	2	12:31	16.9	15.0	0.82	25.5	0.228	50.2	59.8
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Case 5 (Wm. C.)..	Prelim.	11:39	.....	.....	.....	.....	.....	.....	.....
3/2/16 62.9 Kg. 1.83 Sq. M.	1	12:39	20.0	17.0	0.86	22.6	Lost	57.3*	57.4
	2	1:39	21.7	18.1	0.87	24.4	Lost	61.5*	65.7
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Case 6 (John B.)..	Prelim.	11:55	.....	.....	.....	.....	.....	.....	.....
11/4/15 50.5 Kg. 1.48 Sq. M.	1	12:55	16.7	15.5	0.78	21.7	0.268†	51.2	51.4
	2	1:55	16.4	15.8	0.76	21.8	0.268†	52.1	54.3
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....

* Calculated from table of Magnus-Levy, assuming 15 per cent. of calories from protein.
† Calculated from 24-hour specimen.

—Calorimeter Experiments

Direct Calorimetry, Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Lin.)	
.....	37.2	....	.....	.....	..	..	..	....	....	Basal; in bed
69.0	37.1	61	14	0.80	..	..	..	....	....	Very quiet
74.4	36.9	59	11	0.82	..	..	..	....	....	Very quiet
.....	.....	....	.....	.....	22	50	28	0.95	35.6	
.....	37.2	69	.....	.....	..	..	..	....	....	In bed; 18 hours after food
70.1	37.1	69	34	0.81	..	..	..	....	....	Restless, coughing
80.4	37.2	66	34	0.75	..	..	..	....	....	Restless, coughing
.....	.....	....	.....	.....	10	68	22	1.13	41.6	(observation not included in averages)
.....	37.1	74	.....	.....	..	..	..	....	....	Basal; in bed
56.7	36.9	70	7	0.90	..	..	..	....	....	Very quiet
69.4	36.9	70	30	0.84	..	..	..	....	....	Quiet
.....	.....	....	.....	.....	12	39	49	0.95	35.5	
.....	37.4	....	.....	.....	..	..	..	....	....	Basal; in bed
42.7	37.3	72	16	0.81	..	..	..	....	....	Very quiet; 50 min. period
72.0	37.4	74	47	0.80	..	..	..	....	....	Fairly quiet; 70 min. period
.....	.....	....	.....	.....	11	60	29	1.12	35.6	
.....	37.0	....	.....	.....	..	..	..	....	....	Basal; in bed
49.2	36.8	55	4	0.82	12	54	34	....	....	Motionless
56.1	36.7	55	7	0.82	12	65	23	....	....	Almost motionless
.....	.....	....	.....	.....	..	..	..	0.74	27.9	
.....	36.7									
55.1	36.7	66	6	.....	..	..	..	....	....	Very quiet; dozed 45 minutes
66.0	36.7	63	18	.....	..	..	..	....	....	Quiet; awake
.....	.....	....	.....	.....	..	..	..	0.94	34.3	
.....	36.8	....	.....	.....	..	..	..	....	....	Basal; in bed
45.7	36.7	49	28—	0.78	14	64	22	....	....	Fairly quiet
52.5	36.7	51	33—	0.75	14	74	12	....	....	Restless last 10 minutes
.....	.....	....	.....	.....	..	..	..	1.02	34.9	

His mother died at the age of 93. The patient himself has always been rather weak physically. Over twenty-five years ago he had malaria and yellow fever, which caused deafness in the right ear. Ten years ago he discovered that his right eye was almost blind. For the last two or three years his memory has been failing, particularly for recent events. He has been a heavy smoker and when young was moderately alcoholic. At present he has marked nocturia. He kept at his clerical work until July, 1915.

Physical Examination.—Well preserved old man, skin only slightly wrinkled, moderate flabbiness of flesh, slight tremor of hands, gait shuffling. The right eye shows a cataract. The heart is slightly enlarged, with an occasional premature systole. There is a faint systolic murmur at the apex and a rough diastolic murmur. Radials are faintly palpable. The lungs are emphysematous. Blood pressure: systolic, 180 mm.; diastolic, 100 mm. Temperature normal; pulse, 55 to 75.

This patient was becoming senile rather rapidly. At the time of the calorimeter observation he was fairly active and spent some of his time walking about the ward. A month or so later he was almost blind, failing mentally and glad to stay in his chair all day.

DISCUSSION OF RESULTS

The calorimeter findings on the group of old men can be compared directly with the findings on Boy Scouts and normal adults between the ages of 20 and 47. The experimental methods used with all of these subjects were the same in almost all particulars. There was, however, one difference between the groups which could not be avoided. The younger subjects were active men on liberal diets, and almost all of them came to the calorimeter room from their homes on the mornings of the experiments. The old men were beyond the working age, they had been on rather meager fare, and they were all kept in the metabolism ward for several days before the tests were made. All of these factors tend to decrease the total metabolism in the same manner in which cage life affects a dog.[2] Still they are part and parcel of old age. It would be difficult to find hard working men of 80 on large diets, or normal men in the prime of life leading the existence of octogenarians.

If we look at the results of the calorimeter experiments we are struck by their uniformity in five of the observations. The first experiment on Henry L. is published for the sake of completeness, but it cannot be considered a test of the basal metabolism. The old man was stupid and did not understand the instructions to stay quiet. He turned frequently from side to side and inhaled snuff which he had smuggled into the calorimeter. This made him cough and sneeze. The second time he was in the calorimeter he was quiet and the observation was very satisfactory. It will be noted that the metabolism of Charles W. was unusually low. This may be accounted for by the fact that he was much more senile than the others. While this finding is of

2. Lusk, G.: Animal Calorimetry, Paper 11, Jour. Biol. Chem., 1915, **20,** 565; and Allen and Du Bois: Clinical Calorimetry, Paper 17, THE ARCHIVES INT. MED., 1916, **17,** 1056.

TABLE 2.—Old Men. Clinical Data[1]

Case Number Name and Date	Food			Food N., Gm.	Urine N., Gm.	Feces N., Gm.	Excreta N.,[2] Gm.	Nitrogen Balance, Gm.	Body Wt., Kg.	Urine Volume, C.c.	Calories per Kg.	Blood Pressure
	Total Calories	Carbohyd., Gm.	Fat, Gm.									
Case 1 Andrew O'C.												
5/ 7/16	2,354	223	125	10.7	9.1	1.1	10.1	+0.6	....	1,100		
5/ 8/16	2,524	240	135	11.2	9.5	1.1	10.6	+0.6	....	1,675		
5/ 9/16	2,592	278	136	7.2	9.4	0.7	10.1	—2.9	70.2	1,420	37	
5/10/16	2,443	277	130	4.0	7.2	0.4	7.6	—3.6	....	1,760	..	235–100
5/11/16	3,043	445	120	4.0	7.2	0.4	7.6	—3.6	70.2	1,630	29	
5/12/16	3,043	436	125	4.1	4.0	0.4	4.4	—0.4	70.1	1,440	29	
Case 2 Henry L.												
3/10/16	2,766	286	129	15.4	8.8[3]	1.5	10.3	+5.1	....	1,600[3]		
3/11/16	2,885	310	135	13.9	8.2	1.4	9.5	+4.4	69.1	760	42	
3/12/16	2,824	304	129	15.0	9.0[4]	1.5	10.5	+4.5	69.1	1,030[4]	41	
3/13/16	.....	...	...	....	6.1[5]	...	....	.....	67.9	1,037[5]	..	154–80
3/14/16	2,924	323	131	14.7	7.2	1.5	8.7	+6.0	68.7	580	41	
3/15/16	3,511	353	180	14.3	7.5	1.4	8.9	+5.4	69.1	650	50	
3/16/16	3,577	352	186	15.6	10.4	1.6	11.9	+3.7	69.6	960	51	
3/17/16	3,460	326	186	15.4	7.1	1.5	8.6	+6.8	69.5	600	50	
3/18/16	.....	...	...	....	...	...	....	.....	....	.....	..	153–100
Case 3 Charles H.												
5/3/16	1,954	184	101	10.2	7.4	1.0	8.4	+1.8	52.9	1,045	..	210–100
5/4/16	2,299	218	121	11.0	8.2	1.1	9.3	+1.7	53.6	800	43	
Case 4 Charles W.												
5/3/16	2,008	220	92	9.8	6.4	1.0	7.4	+2.4	....	1,480		
5/4/16	1,765	153	97	9.1	7.0	0.9	7.9	+1.2	69.1	1,660	..	180–100
Case 5 William C.												
3/2/16	1,825[7]	191[6]	82	11.0	11.3	...	....	.....	62.9	1,940[6]	29	
Case 6 John B.												Syst.
11/ 4/15	1,364	126	69	7.9	6.6	...	....	.....	50.5	1,230	27	180–190
12/12/15	1,450	195	60	3.4								Diast. 100
12/13/16	1,326	189	51	3.2	4.1	...	....	.....	51.0	700		

1. Temperature normal in all cases throughout the experiments.
2. Excreta nitrogen calculated as urine nitrogen plus 10 per cent. of food nitrogen.
3. Twenty-three hours fifteen minutes.
4. Twenty-three hours thirty minutes.
5. Twenty-three hours thirty minutes.
6. 48.7 gm. glucose in urine.
7. Approximately.

importance in showing the great depression in metabolism which may occur in old age, we are not justified in using it to obtain the average figure which represents the heat production of men of his age. The average for the other five men was 35.1 calories per square meter per hour, and the average deviation from this mean was a little over 1 per cent. When we take the group of fifteen younger men studied in the calorimeter, we find an average deviation from the mean of about 3 per cent. The results on Charles W. show a deviation of 21 per cent. from the average of the other old men. He is therefore excluded from the averages as the result of the rule which debars an observation in which the deviation from the mean is greater than four times the average deviation.

TABLE 3.—Old Men. Summary

Case Number and Name	Age, Yrs.	Weight, Kg.	Height, Cm.	Signs of Senility	Surface Area (Lin.) Sq. M.	Total Calories in 2 Hours		Cal. per Hour		Per Cent. from Adult, Av. 39.7	Av. R. Q.	Av. Pulse
						Indirect	Direct	Per Kg.	Per Sq. M.			
1. Andrew O'C.	77	69.7	171	+	1.87	133.3	143.4	0.962	35.6	—10	0.81	59
2. Henry L.	78	67.9	167	++	1.85	154.0	150.5	1.13	(41.6)*	(+ 5)*	0.78	68
Henry L.	..	68.9	...	....	1.85	130.7	126.1	0.949	35.3	—11	0.86	71
3. Charles H. ..	79	52.9	163	+	1.66	118.0	114.6	1.12	35.6	—10	0.80	73
4. Charles W. ..	80	69.1	164	+++	1.82	101.7	105.3	0.736	27.9†	—30†	0.82	55
5. William C. ..	83	62.9	163	++	1.73	118.8	121.2	0.944	34.3	—14	0.86	65
6. John B.	83	50.5	158	+++	1.48	103.3	98.2	1.02	34.9	—12	0.77	50
Total or aver.	..	....	...	....	.....	859.8	859.3	.....	35.1	....	0.81	

* Excluded from averages on account of restlessness.
† Excluded from averages on account of unusually low metabolism.

The average heat production of the five men between the ages of 77 and 83 was 35.1 calories per square meter per hour, which is about 12 per cent. below the average for men between the ages of 20 and 50. This depression in old age is about 7 per cent. less than had been assumed by one of us in a curve based on results obtained by other investigators.[3] As one might expect, the depression of metabolism is somewhat proportional to the degree of senility.

The respiratory quotients lie between the figures 77 and 86, the average being 81. The method of direct calorimetry gives a total of 859.3 calories for the seven experiments, which is within 0.1 per cent. of the total obtained by the independent method of indirect calorimetry (859.8 calories). This agreement is unusually close for two-hour experiments.

3. Du Bois, E. F.: The Respiration Calorimeter in Clinical Medicine, Am. Jour. Med. Sc., 1916, **151,** 781.

SUMMARY AND CONCLUSIONS

A group of six men between the ages of 77 and 83 were studied in the calorimeter. Their average basal heat production was 35.1 calories per square meter per hour, which is 12 per cent. below the average for men between the ages of 20 and 50. The methods of direct and indirect calorimetry agreed closely and the respiratory quotients were all within normal limits.

NOTE.—At the suggestion of Drs. Means and Boothby, a set of normal standards for various ages has been calculated from the age curve published in this paper and Lusk's "Science of Nutrition," third edition, 1917. These will be used in the Sage publications after the present series, until changes in the curve are made by the addition of new data. The figures for females are calculated as 7 per cent. below the average for males, more data, however, being desirable to establish for the female sex the general validity of this method of computation.

CALORIES PER SQUARE METER OF BODY SURFACE PER HOUR
(HEIGHT-WEIGHT FORMULA)

Age, Years	Males	Females
14-16	46.0	43.0
16-18	43.0	40.0
18-20	41.0	38.0
20-30	39.5	37.0
30-40	39.5	36.5
40-50	38.5	36.0
50-60	37.5	35.0
60-70	36.5	34.0
70-80	35.5	33.0

477 First Avenue.

CLINICAL CALORIMETRY

TWENTIETH PAPER

THE EFFECT OF CAFFEIN ON THE HEAT PRODUCTION*

J. H. MEANS, M.D.,† BOSTON, J. C. AUB, M.D.
AND
E. F. DU BOIS, M.D.
WITH THE TECHNICAL ASSISTANCE OF G. F. SODERSTROM
NEW YORK

The object of this research was to determine the effect of a single large dose of caffein on the respiratory metabolism of normal individuals.

The earliest work on the effect of this drug on the gaseous exchange, so far as we have been able to discover, was that of Hoppe[1] in 1857. He found some increase in the carbon dioxid output after taking caffein, but the conditions of his experiments are open to criticism. He was followed two years later by Smith[2] who studied in a masterly way nearly every aspect of respiration, including the effect of tea, coffee, etc. His technic, so far as one can judge from the description, was excellent. His apparatus was of the open circuit type, the subject breathing through a mask and valves. The inspired air went first through a dry meter and the expired air first through a Woulff bottle, containing pumice stone saturated with sulphuric acid, then through a gutta-percha box having a series of compartments in which the air was exposed, over a large surface, to concentrated potassium hydrate. Next, it was passed through a second Woulff bottle with sulphuric acid, the carbon dioxid was determined by the gain in weight of the absorbers, exactly as is done with the modern calorimeter. The total ventilation of the lungs, the evaporation of moisture from the lungs, the respiration rate and pulse rate were the other factors studied. The oxygen, of course, was not obtained. After taking from 50 to 100 grains of black or green tea leaves, or half an ounce of strong coffee, a rise in the carbon dioxid output was invariably found with

* Submitted for publication Dec. 19, 1916.

* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division, Bellevue Hospital.

† Henry P. Walcott Fellow in Clinical Medicine, Harvard University.

1. Hoppe: Ueber die Wirkungen des Coffein, Deutsch. Klin., 1857, **9,** 181.

2. Smith, Edward: Experimental Inquiries Into the Chemical and Other Phenomena of Respiration and Their Modifications by Various Physical Agencies, Philosophical Transactions, London, 1859, **149,** 681.

several normal subjects. A very large number of experiments were performed. The rise was anywhere from 15 to 30 per cent. and the maximum usually occurred within an hour from the time of taking the drug. An increase in the ventilation of the lungs of similar proportion was also found. The respiratory rate was sometimes increased, sometimes decreased. The pulse was usually slightly accelerated.

The next extensive study of the effect of caffein on the metabolism, so far as we are aware, is that of Reichert[3] in 1890. This observer worked with dogs, his apparatus being a simple type of water calorimeter. The method of direct calorimetry alone was used. His work may be subject to some criticism, for the dogs were tied down and occasionally struggled. The results of his normal control experiments sometimes differed rather widely, but the faults were remedied to some extent by the very large number of experiments made. The caffein was given subcutaneously. A basal hour was secured first and the dogs were then observed for five hours after receiving the drug. Three series of experiments were performed. In the first series the dose was 0.035 gm. per kg. Five experiments were made. The average increase in heat production was 38.6 per cent. Heat elimination was also increased, but in relation to production was inconstant. In three experiments heat elimination was in excess; in the other two it was not. In the second series, 0.07 gm. per kg. were given. The average increase in heat production was 43.6 per cent. The maximum was reached in two experiments during the first hour after administering the drug; in three, during the second hour. In all the experiments of this series, heat production was in excess of elimination during the first hour, and in three, in excess during the subsequent hour. More heat was eliminated than produced during the remaining hours. In the third series, 0.105 gm. per kg. was given. (The lethal dose was from 0.15 to 0.20 gm. per kg.). In this series there was an average increase in heat production of 71.4 per cent. In all the experiments heat production was in excess of elimination in the first hour and in three also in the second hour. In summing up, Reichert says, "These results show beyond possible doubt that caffein increases heat production, and as a corollary, increases destructive tissue metamorphosis."

More recently, Edsall and Means[4] reported experiments on the effect of caffein on two normal men. In one, after 0.324 gm. of caffein

3. Reichert, E. T.: Action of Caffein on Tissue Metamorphosis and Heat Phenomena, New York Med. Jour., 1890, **51,** 456. For a description of his apparatus see Heat Phenomena in Normal Animals, University Med. Mag., Philadelphia, 1890, **2,** 173, 225, 345.

4. Edsall, D. L., and Means, J. H.: Effect of Strychnin, Caffein, Atropin and Camphor on the Respiration and Respiratory Metabolism in Normal Human Subjects, THE ARCHIVES INT. MED., 1914, **14,** 897.

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 1.....	Prelim.	11:32	.....	.....	.....	.....	.....	.....	.....
(E. F. D. B.) 4/12/16	1	12:32	25.4	22.7	0.81	31.5	0.502	75.5	82.4
76.5 Kg. 1.94 Sq. M.	2	1:32	24.7	22.7	0.79	32.7	0.502	75.3	82.0
Av. basal.....	.....	.....	.....	.....	.....	.....	.....	75.4	.....
	3	2:32	27.8	25.7	0.79	37.8	0.688	84.7	87.4
	4	3:32	25.6	23.5*	0.79	37.1	0.688	77.5	82.4
Av. after caffein	.....	.....	.....	.....	.....	.....	.....	.....	.....
E. F. D. B.	Prelim.	11:07	.....	.....	.....	.....	.....	.....	.....
4/25/16 77.3 Kg. 1.95 Sq. M.	1	12:07	24.4	22.1	0.80	33.3	0.536	73.2	78.9
	2	1:07	27.1	Lost	.....	34.7	0.705	83.5†	82.0
	3	2:07	25.9	Lost	.....	35.7	0.705	78.9†	83.3
	4	3:07	25.8	24.6	0.77	33.8	0.579	80.7	79.5
	5	4:07	26.2	23.7	0.81	34.9	0.579	78.6	81.6
Av. after caffein	.....	.....	.....	.....	.....	.....	.....	80.6	.....
Case 2 (J. H. M.)..	Prelim.	11:26	.....	.....	.....	.....	.....	.....	.....
4/21/16 75.3 Kg. 1.89 Sq. M.	1	12:26	24.2	21.9	0.80	32.3	0.524	72.8	81.3
	2	1:26	25.1	23.1	0.79	34.9	0.524	76.4	87.5
Av. basal.....	.....	.....	.....	.....	.....	.....	.....	74.6	.....
	3	2:26	29.5	26.5	0.81	36.1	0.604	88.1	84.3
	4	3:26	28.9	27.3	0.77	41.2	0.604	89.9	90.0
	5	4:26	31.5	29.9	0.77	42.2	0.618	98.4	89.7
Av. after caffein	.....	.....	.....	.....	.....	.....	.....	92.1	.....
Case 3 (J. C. F.)...	Prelim.	11:39	.....	.....	.....	.....	.....	.....	.....
4/27/16 64.3 Kg. 1.75 Sq. M.	1	12:39	23.6	21.2	0.81	26.8	0.592	70.4	70.5
	2	1:39	25.9	22.7	0.83	28.6	0.592	75.7	77.4
Av. basal.....	.....	.....	.....	.....	.....	.....	.....	73.1	.....
	3‡	2:42	26.3	24.7	0.78	36.9	0.631	81.1	87.0
	4§	3:39	25.8	22.8	0.82	41.7	0.516	76.1	81.8
	5	4:39	26.6	23.3	0.83	34.3	0.414	78.0	76.6
Av. after caffein	.....	.....	.....	.....	.....	.....	.....	78.4	.....
Case 4 (J. C. A.)...	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
4/29/16 60.2 Kg. 1.64 Sq. M.	1	12:10	22.3	19.1	0.85	29.6	0.546	64.0	70.3
	2	1:10	22.8	19.2	0.87	29.6	0.546	64.5	72.4
Av. basal.....	.....	.....	.....	.....	.....	.....	.....	64.3	.....
	3	2:10	25.4	21.9	0.84	32.6	0.546	73.4	75.2
	4	3:10	26.4	24.6	0.78	38.4	0.546	81.2	81.6
	5	4:10	22.6	20.2	0.81	33.4	0.546	66.9	73.1
Av. after caffein	.....	.....	.....	.....	.....	.....	.....	73.8	.....

* Small leak found in blower this hour.
† Calculated from CO_2, R. Q. assumed to be 0.79.
‡ 63-minute period.
§ 57-minute period.

—Calorimeter Experiments

Direct Calorimetry Calories	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
.....	36.9	62								
80.8	36.8	56	9	0.82	..	..	..	....	38.9	Basal; very quiet; on right side
81.0	36.8	58	24	0.79	..	..	..	....	38.8	Basal; very quiet; on back
.....	.....	....	.....	.....	18	56	26	0.99	38.8	Caffein, 0.65 gm. at 1:33 p. m.
89.1	36.9	56	22	0.78	22	58	20	....	43.6	Very quiet
81.5	36.9	55	14	0.79	24	55	21	....	40.0	Very quiet
.....	.....	....	.....	.....	..	..	..	....	41.8	
.....	36.9									
71.5	36.8	56	28	0.80	19	54	27	0.95	37.5	Basal; quiet
78.5	36.8	55	30	.....	..	..	..	....	42.8	Caffein, 0.65 gm. at 12:08 p. m.; quiet
86.3	36.9	60	13	.....	..	..	..	....	41.0	Very quiet; on right side
79.8	36.9	55	11	0.76	19	67	14	....	41.4	Very quiet; on back
82.4	37.0	56	21	0.81	20	53	27	....	40.3	Quiet
.....	.....	....	.....	.....	..	..	..	1.04	41.4	
.....	36.9									
71.6	36.7	59	26	0.80	..	..	..	....	38.5	Basal; fairly quiet
83.4	36.7	55	30	0.79	..	..	..	....	40.4	Basal; fairly quiet
.....	.....	....	.....	.....	19	57	24	0.99	39.5	Caffein, 0.65 gm. at 1:27 p. m.
90.4	36.8	57	21	0.81	18	53	29	....	46.6	Fairly quiet
92.6	36.9	62	32	0.76	18	67	15	....	47.5	Fairly quiet
96.5	37.0	77	39	0.76	17	68	15	....	52.0	Fairly quiet
.....	.....	....	.....	.....	18	63	19	....	48.8	
.....	36.3									
71.2	36.3	....	19	0.81	22	50	28	....	40.2	Basal; very quiet
78.0	36.4	....	45	0.84	21	43	36	....	43.3	Fairly quiet; reading
.....	.....	....	.....	.....	22	46	32	1.14	41.7	Caffein, 0.54 gm. at 1:43 p. m.
81.5	36.3	....	33	0.77	22	62	16	....	46.4‡	Very quiet
73.8	36.2	....	33	0.83	17	49	34	....	43.5§	Very quiet; slept 25 minutes
77.0	36.3	....	32	0.84	14	48	38	....	44.5	Very quiet
.....	.....	....	.....	.....	18	53	29	....	44.8	
.....	36.8									
75.9	36.9	66	18	0.86	..	..	..	....	39.0	Basal; very quiet
73.6	36.9	65	9	0.89	..	..	..	....	39.3	Basal; very quiet
.....	.....	....	.....	.....	..	..	..	1.07	39.1	Caffein, 0.525 gm. at 1:11 p. m.
74.0	36.9	61	21	0.85	..	..	..	....	....	Fairly quiet
80.6	36.9	59	46	0.77	..	..	..	....	49.5	Fairly quiet
67.7	36.8	59	18	0.82	..	..	..	....	40.7	Very quiet
.....	.....	....	.....	.....	23¶	38¶	44¶	1.23	45.0	

¶ Average of whole experiment.

sodium salicylate, given subcutaneously, there was an average rise of 10.6 per cent. in the metabolism, as measured by indirect calorimetry. The maximum of 13.9 per cent. was reached in the first hour. With the other subject there was an average rise of 3 per cent. and a maximum of 5.7 per cent. after 0.39 gm., given in the same way.

Higgins and Means[5] obtained similar results. In one normal subject, after 0.32 gm. of caffein sodium benzoate subcutaneously there was an average rise of 13.8 per cent. in the indirect calorimetry. The maximum rise of 15.4 per cent. occurred within the first hour. In another normal subject, 0.32 gm. of the same drug was given subcutaneously and was followed by an average rise of 4.5 per cent. and a maximum of 7.2 per cent., which occurred during the second hour.

In neither Edsall and Means' nor in Higgins and Means' experiments was there any consistent change in the respiratory quotient after the drug; in other words, the proportion of fat, carbohydrate and protein utilized showed no regular deviation from the normal.

METHODS OF EXPERIMENTS

Five calorimeter experiments on four normal men were carried out in precisely the same way as already described in the preceding papers of this series.[6] The surface area of all the subjects was determined by the so-called "Linear Formula," described in Papers 5, 9 and 10. The calories derived from protein were calculated from specimens voided between the hours of 8 a. m. and 5 p. m.

The caffein was taken in the form of the pure alkaloid dissolved in water. A tumbler containing the caffein dissolved in 300 c.c. of water at room temperature was placed in the calorimeter when the subject entered. After a preliminary period and one or two hours of observation of the subject's normal basal metabolism, he was told to drink the mixture and was allowed to follow it with a little pure water. After the taking of the drug the observation was continued for three hours, except in one experiment, when the third hour was omitted.

The subjects were studied in the morning hours at complete rest, fourteen to eighteen hours after the last meal. They were not allowed to take coffee or tea for the twenty-four hours previous to the test.

The data of all the experiments are given in the accompanying table.

DESCRIPTION OF SUBJECTS OF EXPERIMENTS

CASE 1.—E. F. D. B., man, aged 34, height 178 cm., physician. For history see Fourth Paper of this series. Since last year he has been in good health; has taken very little exercise since September, 1915. Takes one medium-sized

5. Higgins, H. L., and Means, J. H.: Effect of Certain Drugs on the Respiration and Gaseous Metabolism of Normal Human Subjects, Jour. Pharmacol. and Exper. Therap., 1915, **7**, 1.

6. Papers 1 to 8: THE ARCHIVES INT. MED., 1915, **15**, 793-944; Papers 9 to 17: Ibid., 1916, Part 2, **17**, 855-1059.

cup of coffee at breakfast and occasionally tea in the afternoon, or a small cup of coffee after dinner. Is kept awake by coffee or tea taken after 1 p. m. Tobacco, moderate. Alcohol, occasionally in small amounts.

CASE 2.—J. H. M., man, aged 31, height 177 cm., physician. Measles, mumps, scarlet fever and chickenpox in childhood; a bronchopneumonia at 26 and paratyphoid at 28; otherwise, has always enjoyed good health. Takes exercise only spasmodically, but leads a fairly active life.

Takes one cup of coffee in the morning about half the time, a small cup of coffee after dinner about twice a week, one or two cups of tea in the afternoon about four times a week. One demitasse will not keep him awake; a large cup of coffee in the evening will. Tobacco, moderate. Alcohol, occasionally in small amounts.

CASE 3.—J. C. F., man, aged 23, height 178 cm., chemist. Pleurisy and pneumonia at 6; scarlet fever at 13; occasional sore throat. In good health except for slight nasal obstruction. Exercise: walks three to four miles a day.

He takes a cup of coffee at each meal and sometimes a cup late at night without being kept awake. Tobacco, three to five cigars a day. Alcohol, none.

CASE 4.—J. C. A., man, aged 26, height 175.2 cm., physician. Scarlet fever nine years ago; catarrhal jaundice five years ago; in good health since. Leads a sedentary life, but always takes some exercise.

Takes two cups of coffee a day; no tea. Even large quantities of coffee in the evening never keep him awake. Tobacco, ten cigarets a day. Alcohol, occasionally in small amounts.

DISCUSSION OF RESULTS

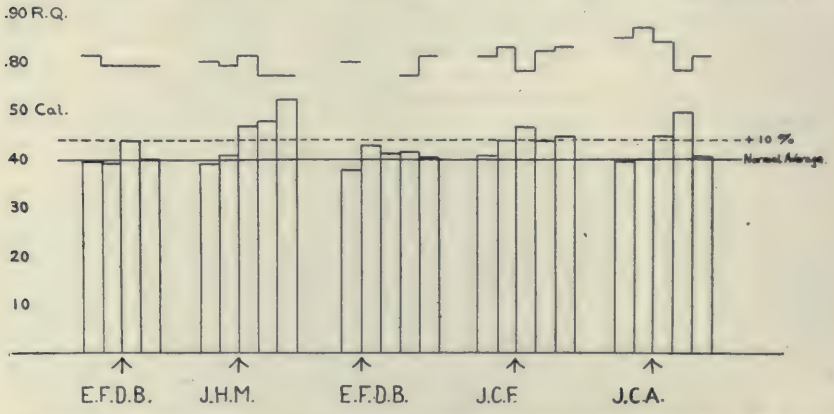
The Basal Metabolism After Giving Caffein.—This was increased in each experiment. The dose given, 8 to 10 grains, approximately 8.6 mg. per kg. of body weight, is considerably larger than the usual therapeutic dose. In all five experiments there was a rise in the basal metabolism (indirect calorimetry). This rise varied from the minimum of 11.3 per cent. with J. C. F., to the maximum of 31.6 per cent. with J. H. M. The highest average rise was that of J. H. M., 23.5 per cent., and the lowest that of J. C. F., of 7.4 per cent. In three experiments, both those on E. F. D. B. and that on J. C. F., the maximum rise occurred in the first hour after receiving the drug. In the experiment on J. C. A., the maximum rise occurred in the second hour, and that in J. H. M. in the third hour. In none of these experiments had the metabolism returned to the basal value when the observation was discontinued. The increments in the metabolism obtained in this series of experiments are definitely greater than those obtained by Edsall and Means and by Higgins and Means when using much smaller doses of the drug. The rises in the basal metabolism of the present experiments are shown graphically in the accompanying figure.

As one looks over the enormous literature on the various actions of caffein, one gets the impression that the numerous contradictory statements are not necessarily due entirely to faulty observation, but possibly because the action of caffein on any given function is extremely variable, often diametrically opposite, in different individuals, and in the same individual with varying dosage. Nevertheless, the present

series of experiments, together with those in the literature, show that an elevation in the basal metabolism is a very frequent action, although its intensity varies considerably in different individuals. In general, there seems to be a larger rise with larger doses.

The Respiratory Quotients.—These show no consistent change in either direction after the drug had been taken.

The Methods of Direct and Indirect Calorimetry. — These agree closely in the hours following the taking of caffein. The total calories as measured by the former method in the hours following the drug were 1,230.3. This is within 1 per cent. of the total of 1,218.0 calories as measured by the method of indirect calorimetry. This agreement of two absolutely independent methods is unusually close, and it confirms the technical accuracy of the findings. The drug had little effect on



Results shown graphically. Columns represent calories per hour as measured by indirect calorimetry. Arrows indicate point at which the caffein was taken. The topmost lines show the respiratory quotients.

the body temperature and the differences between heat elimination and heat production are such as would be found in experiments on normal controls.

The agreement between the methods of direct and indirect calorimetry in the basal hours before the drug was taken is not very close. The direct method gives a total of 687.6 calories; the indirect, 647.8 calories. The method of direct calorimetry is seldom very satisfactory in the first hour of an observation, and these one- or two-hour basal experiments are not long enough to balance up the inequalities. With longer experiments on normal controls the agreement is within a fraction of 1 per cent., as has been shown in previous papers.

The Elimination of Water from Skin and Lungs. — This was increased, after taking the caffein, in every experiment. This was greatest in the case of J. C. F., being 36 per cent. and least in the second

experiment on E. F. D. B., when it was but 5 per cent. The average percentage of calories lost in the vaporization of water during the basal hours was 24.1 per cent.; after taking the caffein the average was 26.3 per cent. The drug affects but slightly the mechanism by which the body dissipates heat in response to an increased heat production.

Nitrogen Elimination.—The total nitrogen in the urine showed a rise after taking caffein in each experiment except that on J. C. A., when the data were not obtained. This rise was greatest in the first experiment on E. F. D. B., 37 per cent., and next greatest in the second experiment on the same subject, 31 per cent. It was least in the case of J. C. F., 6 per cent. J. C. F. likewise had the least rise in basal metabolism, but E. F. D. B. did not have the greatest. This increase might have been merely the washing out of nitrogenous bodies as a result of the caffein diuresis.

The Pulse Rate.—This showed sometimes a slight rise, sometimes a slight fall, or else no change at all after the subject received the drug.

SUMMARY

An increase of from 7 to 23 per cent. in the basal metabolism was found in four normal subjects after receiving 8 to 10 grains of caffein alkaloid (8.6 mg. per kg. of body weight). After taking the drug there was no significant change in the pulse rate, in the respiratory quotient, in the proportions of the various foodstuffs metabolized, or in the percentage of heat lost in the vaporization of water. The independent methods of direct and indirect calorimetry gave results which agreed within 1 per cent.

477 First Avenue.

CLINICAL CALORIMETRY

TWENTY-FIRST PAPER

THE BASAL METABOLISM OF DWARFS AND LEGLESS MEN WITH OBSERVATIONS ON THE SPECIFIC DYNAMIC ACTION OF PROTEIN*

JOSEPH C. AUB, M.D., AND EUGENE F. DU BOIS, M.D.

WITH THE TECHNICAL ASSISTANCE OF G. F. SODERSTROM

NEW YORK

In order to establish more fully the law that the total body metabolism is proportional to the surface area, it is important to establish the law not only for people of normal size and shape, but also for those who are deformed. If the body surface be a true index of the metabolism, and if the body surface be accurately measured, then dwarfs or men with their legs cut off would show proportionally the same basal metabolism per square meter of surface as do normally shaped individuals. But if this relationship holds, is the increase in heat production which follows the ingestion of large quantities of meat the same as in persons of normal shape? It was to try to answer these questions that this series of dwarfs and legless men were studied in the Sage calorimeter at Bellevue Hospital.

THE BASAL METABOLISM OF MEN OF UNUSUAL SHAPE

History.—The basal metabolism of normal individuals has been well established by the large number of normal controls gathered by Benedict, Emmes, Roth and Smith;[1] by Means[2] and by Gephart and Du Bois.[3] The total metabolism of dwarfs has been investigated in one case each by Rubner[4] and by McCrudden and Lusk.[5]

Rubner studied a very small dwarf who was 20 years old and

* Submitted for publication Dec. 26, 1916.

* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division, Bellevue Hospital.

1. Benedict, F. G., Emmes, L. E., Roth, P., and Smith, H. M.: The Basal Gaseous Metabolism of Normal Men and Women, Jour. Biol Chem., 1914, **18,** 139.
2. Means, J. H.: Basal Metabolism and Body Surface, Jour. Biol. Chem., 1915, **21,** 263.
3. Gephart, F. C., and Du Bois, E. F.: The Determinations of the Basal Metabolism of Normal Men and the Effect of Food, THE ARCHIVES INT. MED., 1915, **15,** Part 2, p. 835.
4. Rubner, M.: Biologische Gesetze, Marburg, 1887, p. 10; Beiträge zur Ernährung im Knabenalter, Berlin, 1902, p. 45.
5. McCrudden and Lusk: The Metabolism of a Dwarf, Jour. Biol Chem., 1912-1913, **13,** 447.

weighed but 6.6 kg., and who "behaved like a fully grown man." His observations were not made under conditions of complete rest, and so are not comparable to our findings. Rubner, however, calculated that the metabolism per square meter, using Meeh's formula, was but slightly higher than that of a breast-fed infant of similar weight. "The larger metabolism of the dwarf," he writes, "is explained by his greater activity, while the infant is very quiet . . . and neither stands nor walks." This showed, according to Rubner, that metabolism was dependent on surface area, not on age.

McCrudden and Lusk's case was in a boy of 17 years, 113 cm. tall and weighing 21.3 kg. By the height-weight chart his surface area is, therefore, 0.8 square meters. He was a patient described by C. A. Herter[6] under the diagnosis of intestinal infantilism. This is a condition in which the arrest of growth is associated with a group of symptoms based on chronic intestinal intoxication. It is associated with fair mental development, marked abdominal distention, moderate anemia, but most strikingly by frequent periods of diarrhea with fatty and putrefying stools. No definite history of this patient is given, but it is one of the cases used by Herter in the description of the syndrome. Practically normal urinary findings on the same case are reported by McCrudden.[7] The patient was studied in a small calorimeter in Dr. Lusk's laboratory, and the routine was practically the same as is now followed in the Sage calorimeter. The results are, therefore, directly comparable to those reported in this paper. Five observations were made on the dwarf, but only one was a true basal experiment, while on the other occasions he had small amounts of food before entering the calorimeter. The one basal observation has been summarized in Table 1, and shows a normal metabolism per square meter of surface area.

In this series we wish to report the metabolism of five dwarfs; two of the achondroplastic type, one rachitic and two with involvement of the glands of internal secretion. Added to this group are two men who had lost both legs. The basal observations in the calorimeter were made in the routine way followed in this laboratory, and fully described in the third and fourth papers of this series.[8] The subjects had had no food for at least fifteen hours, and during the observation remained quietly lying on a bed.

6. Herter, C. A.: On Infantilism from Chronic Intestinal Infection, 1908.

7. McCrudden: Chemical Studies on Intestinal Infantilism, Jour. Exper. Med., 1912, **15,** 107. McCrudden and Fales: Ibid., 1912, **15,** 113.

8. Gephart, F. C., and Du Bois, E. F.: The Organization of a Small Metabolism Ward, The Archives Int. Med., 1915, **15,** 829. Determination of the Basal Metabolism of Normal Men and the Effect of Food, ibid., p. 834.

We have followed Rischbieth's[9] classification of dwarfs, so careful description of types will not be discussed here. The differentiation of the rachitic, the achondroplastic and the ateliotic (the perfectly proportioned) types is not difficult with the help of the Roentgen ray. However, we have been puzzled in the distinction between the myxedematous and true dwarfism (or ateliotic) types. The skeleton of the ateliotic dwarfs has the same characteristics of bone formation as has the mild cretin, for the cartilage disks of the long bones (according to Rischbieth, and Sternberg[10]) persist throughout life, and the square shaped skull and cretinoid facial appearance may also be present. Both have defective sexual development and both may be mentally defective. Brissaud[11] classifies myxedema, ateliosis and infantilism in one group and Sternberg admits that this is a possible classification. This difficulty in diagnosis confronted us several times in choosing suitable subjects for the investigation.

CASE HISTORIES

CASE 1.—Raphael De P. (Figs. 1 and 2), achondroplastic dwarf, born in Italy, aged 35; a kitchen helper; height 134.7 cm.; weight 40.9 kg.

History.—The family history is negative; no other dwarf in the family for three generations. Had severe illness when a few months old. Since then always well except for chancroid infection twelve years prior to the test. Has been married for eight years to a woman of normal size; has two children, both of normal size.

Physical Examination.—An active, cheerful Italian of normal mentality. The physical examination is negative save for the extremities. All the long bones seem shortened, with slight outward bowing and proportionally large epiphyses. The thighs and upper arms are particularly short. The muscles are powerful. Hands are flat and short, fingers are fat and stubby. Urine, negative. Blood pressure: systolic 120 mm.; diastolic, 90 mm.

CASE 2.—George F.,* hypopituitarism; myxedema; born in Ireland, aged 48; single; a clerk; height 148.8 cm.; weight 53.1 kg.

History.—The family history is negative. He has always been small in stature, though active. For six years he has had occasional attacks of edema, particularly about the eyes, feet and hands. For three years he has had slight shortness of breath and failing vision. He sleeps a great deal and perspires very little. He has had no sexual power for many years.

Physical Examination.—A short, rather fat individual with cretinoid face and feminine type of body. The genitalia are small, the breasts are large. There is no hair except on the head and eyebrows, and this is dry and slightly coarse.

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9. Rischbieth, H., and Barrington, A.: Dwarfism, Treasury of Human Inheritance, London, 1912, Part VII, Sec. xv A.

10. Sternberg, M.: Vegetationsstörungen und Systemerkrankungen der Knochen, Wien., 1899; Nothnagel's specielle Pathologie und Therapie, Vienna, 1903, **7**, Part 2.

11. Brissaud, E.: De l'infantilisme myxedemateux, Nuov. iconog. de la Salpêtrière, 1897, **10**, 240-282.

* This patient was carefully studied by Dr. W. M. Krause, who reported the case in the Jour. Nerv. and Ment. Dis., 1917, **45**, 193.

The arms are long, the hands of trident type. There was general edema without much pitting on admission, but after a week in the hospital this disappeared, leaving a yellowish, dry, much wrinkled skin. Mentally, he is like a well-behaved child and is always good-natured.

Laboratory Findings.—Blood, normal. Urine occasionally showed small amounts of albumin and rare granular casts; 4,000 c.c. of water intake daily for ten days caused no increase in weight. Phenolsulphonephthalein test, 55 and 63 per cent. in two hours. Wassermann negative. Glucose sugar tolerance,

Figure 1

Figure 2

Fig. 1.—Raphael deP. Achondrodystrophy. The meter stick is opposite the spine.

Fig. 2.—Raphael deP. and a dwarf of ateliotic type.

more than 400 gm. Roentgenogram of hands showed epiphyseal ends of bones to be atrophic. The epiphyseal lines are still visible, particularly the lower ends of the radius and ulna. The head shows a markedly enlarged and somewhat eroded sella turcica.

Case 3.—Samuel G., achondroplastic dwarf, born in Germany, aged 29; single; an actor; height 123.5 cm.; weight 34.9 kg.

History.—The family history is negative. His arms and legs have always been very short for his age. Except for an occasional attack of nausea and vomiting, he is perfectly well. Mentally, he is slow and defective; sexually, he is well developed.

Physical Examination.—Negative, save for the extremities. The torso is of normal shape and size; the arms and legs very short. The head is large and square, with a high forehead and a saddle-shaped nose. The hard palate is high. The extremities are very short, particularly the upper arms and legs, but the muscular development is good. The feet and hands are almost normal size and large for the rest of the extremities. The genitalia are of mature development, the body hair is abundant and of normal masculine distribution. The urine is normal.

Case 4.—Patrick W. (Figs. 3, 4, 5 and 6), rachitic dwarf, born in United States, aged 38; actor; height 123.8 cm.; weight 37.3 kg.

Fig. 3.—Pat W., rachitic dwarf.

Patient says he was normal until 3 years old when he became moody and his body became distorted. He had walked and talked at the usual age. He has had gonorrhea three times; twelve years prior to the test he had syphilis, followed by very severe nephritis. During this attack he was very edematous and the abdomen was tapped eight times. Since then he has felt perfectly well.

Physical Examination.—A small, misshapen dwarf with marked curvature of the spine and the longer bones. The head appears normal. The chest is very narrow in the upper portion, with a prominent sternum. There is marked flaring of the lower ribs, with Huntington's groove and marked rosary. The spine shows left lateral curvature in the lower thoracic region, with a slight kyphosis. The legs are very short and markedly bent. The feet appear normal.

The arms are short, but the bones are only slightly curved. The epiphyses of all the long bones are large. The genitalia are well developed; the body hair is of masculine type of distribution.

Laboratory Findings.—Urine was negative; specific gravity, 1.025; albumin, negative. Microscopic examination, negative.

CASE 5.—Irwin E., myxedematous dwarf, born in United States, aged 32; actor; height 134 cm.; weight 37.4 kg.

History.—He has always been of small size. At 10 years of age he was short and weighed but 40 pounds. His school work was not very good, as he failed four times in grammar school. He passed for high school when he was

Fig. 4.—Pat W.

15 years old, and stayed there only one year. He is sexually mature, but inactive. The hair on his head has always been soft and plentiful. He perspires freely.

Physical Examination.—He appears like a well developed boy of 14 years. The facies suggests cretinism—thick eyebrows, puffy eyelids, broad nose, wide maxillae, broad jaw and large, widely spaced teeth. There is a pad of fat between the shoulders and a slight degree of adiposity. The hands are short and stubby; the skin slightly dry, but soft and smooth. The genitalia appear normally developed, but the secondary characteristics are scant for there is no hair on the face, in the axillae or on the body, and the pubic hair is of the feminine configuration. The voice is that of male puberty. Otherwise the

physical examination is not remarkable. Blood pressure: systolic, 95 mm.; diastolic 65 mm.

Roentgenogram of head shows a slightly enlarged sella turcica. In the hand there is some hypo-atrophy of the terminal tufts of the phalanges. The epiphyses of the radius and ulna are not united. The epiphyseal lines of the phalanges are clear.

Case 6.—Harry J. (Fig. 7, described in Paper 9), a legless man, born in the United States, colored, aged 34; beggar. Length is approximately 103 cm., weight 54.6 kg.

Fig. 5.—Pat W. Roentgenogram of knee.

History.—Both legs were cut off by a train when the patient was 6 years old, and since then he has propelled himself on wheels. Seven years prior to the test the right side of the body suddenly became numb and the right arm was completely paralyzed. Slight power returned slowly. He had urethritis seven years previous to the examination, possibly with a chancre, though no secondary manifestations developed.

Physical Examination.—Very muscular negro with short leg stumps. *Face:* Forehead is normal but right side of face is paralyzed; mouth droops and tongue deviates slightly to right. *Chest* is unusually broad and deep, with very powerful muscles in the back, neck and left shoulder and arm. The waist is very narrow; the hips narrow, with poorly developed muscles. The right arm is paralyzed and the muscles are of moderate size but flabby. The

Fig. 6.—Pat W. Spine.

reflexes are exaggerated. The right leg is a very short stump with flabby muscles. The left leg is amputated just above the knee and the stump tapers sharply from the perineal level. The muscles are small and weak. Blood pressure: systolic, 188 mm.; diastolic, 130 mm.

Urine, negative. *Wassermann*, negative.

Case 7.—Robert L. (described in Paper 9), a legless man, born in the United States, aged 43; beggar; length about 125 cm.; weight 63.8 kg.

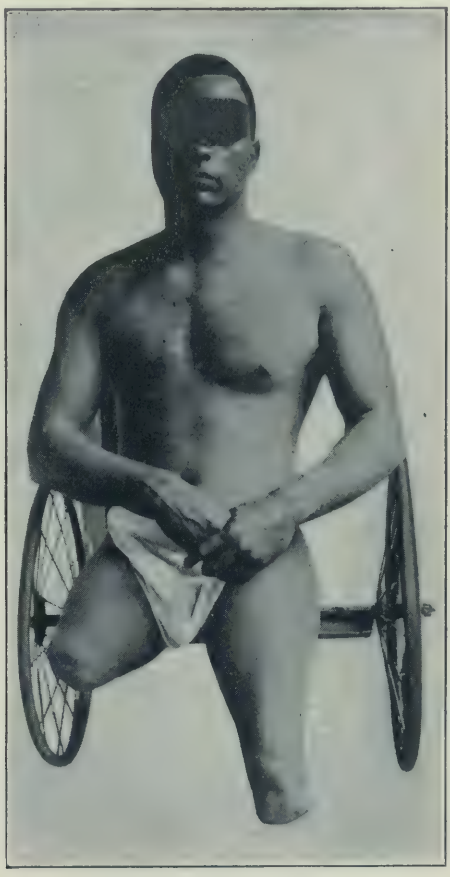

Fig. 7.—Harry J.

History.—The patient was a boiler maker for over twenty years and was always healthy and strong. He had syphilis and urethritis nineteen years ago, for which he received treatment for five months. Five years prior to the examination he was hit by a railroad train and both his legs had to be amputated. He now feels well and supports himself by selling pencils. He walks about a mile every day, with crutches.

Physical Examination.—A heavily built, healthy looking man with fat cheeks and prominent abdomen. His chest is large; his arms muscular. The left thigh is cut off just below the level of the perineum. The right leg is cut off just below the level of the knee and the thigh muscles are firm and strong. Otherwise, the patient appears normal, except that over the left lung there are heard many dry, crackling râles, though resonance, tactile fremitus, vocal fremitus and breath sounds are normal.

TABLE 1.—SUMMARY

Case Number and Name	Subject	Age	Height, Cm.	Weight, Kg.	Surface Area, Sq. M. Linear Formula	Calories per Sq. M. per Hour	Variations from Average Normal 39.7 %	Average R. Q.	Total Calories Measured		Divergence of Direct from Indirect, Per Cent.	Average Calories per Hour, Indirect
									Indirect	Direct		
6. Harry J.*	Legless man	35	103±	54.61	1.34	41.3	+4.0	0.80	110.67	106.42	—3.9	55.34
7. Robert L.	Legless man	43	125±	63.81	1.43	41.3	+4.0	0.80	176.90	178.22	+0.7	58.97
4. Patrick W. ...	Rachitic dwarf	38	123.8	37.31	1.20	41.0	+3.0	0.81	98.27	97.74	—0.5	49.17
1. Raphael DeP.	Achondroplasia	35	134.7	40.86	1.24	42.2	+6.3	0.81	104.66	102.20	—2.3	52.33
3. Samuel G.†....	Achondroplasia	29	123.5	34.92	1.03	(48.9)	(+23.0)	(0.82)	(39.58)	(38.26)	—3.3	52.76
5. Irwin E.	Myxedema	32	134.0	37.37	1.17	29.5	—25.7	0.85	68.98	70.31	+1.9	34.49
2. George F.	{Hypopituitary Hypothyroid	48	148.9	53.05	1.51	31.1	—22.0	0.83	96.57	94.51	—2.1	48.28
J P.‡.....	{"Intestinal Infantilism"	17	113.3	21.3	0.8	38.2	—4.0	0.79	61.12			

* Quiet experiment. 5/6/16.
† Forty-five-minute period only. Nauseated. Other observations two hours.
‡ McCrudden and Lusk's case.

DISCUSSION OF RESULTS

Two of the experiments here recorded were technically unsatisfactory and cannot be considered as giving accurate evidence as to the level of the basal metabolism. The achondroplastic dwarf, Samuel G., was nauseated in the calorimeter and the high figures obtained in his brief observation might have been due to the same factor which caused his vomiting. The legless negro, Harry J., was also restless the first time he was in the calorimeter. While he did not move often, his deformity and paralysis of the right arm made each movement a great exertion. In his second experiment he was quiet and the results were satisfactory.

This leaves good determinations of the basal metabolism of seven men of unusual body shape. Five give figures within the normal limits when the results are calculated according to the surface area. These individuals are the two legless men, Harry J. and Robert L., the rachitic dwarf, Patrick W., the achondroplastic dwarf, Raphael de P., and the dwarf, J. P., with intestinal infantilism, described by McCrudden and Lusk. Two dwarfs give results distinctly below the normal. These are Irwin E. and George F., both of whom had many of the characteristics of cretinism, a condition which is always accompanied by a diminution in the heat production.

It therefore seems true that people with abnormal body shape, but with normal glands of internal secretion, have a metabolism which conforms to their surface area. It is therefore possible that the height of metabolism may be a method for differentiating the ateliotic and myxedematous dwarfs.

THE SPECIFIC DYNAMIC ACTION OF PROTEIN

Many investigators have studied the increased heat production which accompanies the metabolism of protein. The literature has been thoroughly reviewed and discussed by Lusk[12] in his book on nutrition, so that only the most important references are given here.

Von Mering and Zuntz[13] believed that the increased metabolism was due to intestinal work following ingestion of food. This was disproved, however, by the fact that fat and carbohydrate increase metabolism far less than an equal quantity of protein. Rubner[14] and Magnus-Levy[15]

12. Lusk, G.: The Elements of the Science of Nutrition, Ed. 3, Philadelphia, 1917.

13. Von Mering and Zuntz, N.: In wiefern beeinflusst Nährungszufuhr die thierischen Oxydationsprocesse, Pflüger's Arch. f. d. ges Physiol., 1877, **15,** 634.

14. Rubner, Max: Die Gesetze des Energieverbrauchs bei Ernährung, Leipzig, 1902.

15. Magnus-Levy, Ad.: Ueber die Grösse des respiratorischen Gaswechsels unter dem Einfluss der Nährungsaufnahme, Pflüger's Arch. f. d. ges. Physiol., 1894, **55,** 1.

fed bones to a dog and obtained but slight increase in metabolism in spite of the intestinal irritation and activity. Rubner[14] believed that this "specific dynamic action" was due to the cleavages and oxidations necessary to make the foodstuffs available for use by the body cells. The heat given off by these preliminary reactions constituted the waste heat of the dynamic action. In the case of protein, part of the heat, he thought, was derived from the carbohydrate portion burned, but chiefly it arose from the chemical reactions of the remainder of the protein molecule, whose end-products appear in the urine, mostly as urea. This energy, he thought, was liberated unused by the organism. Voit[16] believed that the cells of the body were stimulated to a higher metabolism by food being brought to them. Lusk[17] gave amino-acids and glucose to normal and phlorhizinized dogs. The metabolism of the normal dog was stimulated by both foodstuffs, but the phlorhizinized dog had no change in metabolism when glucose was administered and totally excreted. However, the amino-acids, glycocol and alanin, though unoxidized and excreted with all their energy as sugar and urea, still caused an increase of metabolism. The conclusion is clear that it is not the energy contents of the amino-acids themselves, for those were excreted, but, to quote from the original, "that intermediary products, such as glycollic acid or lactic acid, provide the stimulus. These experiments afford conclusive proof of a true chemical stimulation of protoplasm within the mammalian organism, and offer a logical explanation of the specific dynamic action of protein."

It was to find out where this chemical stimulation occurred, whether in the muscles or in the internal organs, that the following experiments were made at the suggestion of Dr. Lusk. Individuals were taken with normal torsos, but a marked variation in the size of their extremities. If the specific dynamic action of a test protein meal were due to the muscle volume or the surface area, then an achondroplastic dwarf and legless man should show a proportionally smaller stimulation of metabolism than did the normal controls. If the action were due to one of the internal organs, the response of all the subjects tested should be approximately the same.

The subjects chosen were a legless man, an achondroplastic dwarf and three normal controls whose weight closely approximated that of the two abnormal cases. The basal metabolism was determined, following the usual routine technic of this laboratory, fifteen to eighteen hours after the last food. Within the next week the subject was prepared as for a basal observation, but in the morning he was given a

16. Voit, C.: Physiologie des Stoffwechsels und der Ehnährung, Leipzig, 1881, p. 308.

17. Lusk, G.: Animal Calorimetry, XI, An Investigation Into the Causes of the Specific Dynamic Action of the Foodstuffs, Jour. Biol. Chem., 1915, **20,** 555.

large protein meal. This consisted in all cases, except that of Louis M., of about 660 gm. of thoroughly scraped lean beefsteak, chopped very fine and cooked only superficially. In each case a sample was analyzed for protein and fat. A small amount of stewed tomatoes and "Kaffee Hag" were allowed in order to make the food more palatable. Louis M., whose observations are taken from the work of Gephart and Du Bois,[18] had been given the same meal with the addition of 100 gm. of fat. When the subject had finished eating he was put in the calorimeter, and two hours after the start of the meal the observation was begun In several cases the metabolism was also determined for a thirty-minute period, starting one and one-half hours after the start of the meal. All of the subjects received approximately the same amount of protein (24 gm. of nitrogen) and the temperature of the calorimeter was the same for all observations, so that the results are directly comparable; for Rubner[14] pointed out that a change in temperature has a marked effect on the specific dynamic action of protein, and Gigon[19] claimed that the dynamic action did not vary directly with the amount of protein ingested.

The urine was collected in hourly periods, when this was possible, and each sample was analyzed separately for nitrogen, and in most observations for sulphur. In this way the speed of the nitrogen and sulphur excretion could be compared with the increase in metabolism (Table 2). The urinary nitrogen was determined by the usual Kjeldahl method and the sulphur by Benedict's method. The amount of protein and fat ingested was calculated from analyses of each sample of steak used.

CASE HISTORIES

Case 8.—S. K., normal control, born in Japan, aged 33; medical student; height 161.5 cm.; weight 49.5 kg.

The history is entirely negative, except that fifteen years prior to examination he had slight symptoms of beriberi, which rapidly disappeared when he changed his diet. He exercises a great deal, mostly at jiu jutsu and wrestling.

The physical examination is negative. He is a Japanese of very marked muscular development and good physique.

Case 9.—G. T. B., normal control, born in the United States, aged 25; medical student; height 164.5 cm., weight 54.4 kg.

He has always been fairly well, but never athletic or very strong. His life has been a sedentary one, particularly for some months previous to the test, during which he has been studying for examinations.

The physical examination is negative.

Case 10.—Louis M.,[18] normal control, born in Germany, aged 22 years; barber; weight 51.7 kg.

A short, thin, normal individual with small frame and muscles.

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18. Gephart, F. C., and Du Bois, E. F.: Determination of the Basal Metabolism of Normal Men and the Effect of Food, Clinical Calorimetry, Fourth Paper, The Archives Int. Med., 1915, **15,** 835.

19. Gigon, Alfred: Ueber den Einfluss der Nahrungsaufnahme auf den Gaswechsel, Arch. f. Physiol., 1911, **140,** 544.

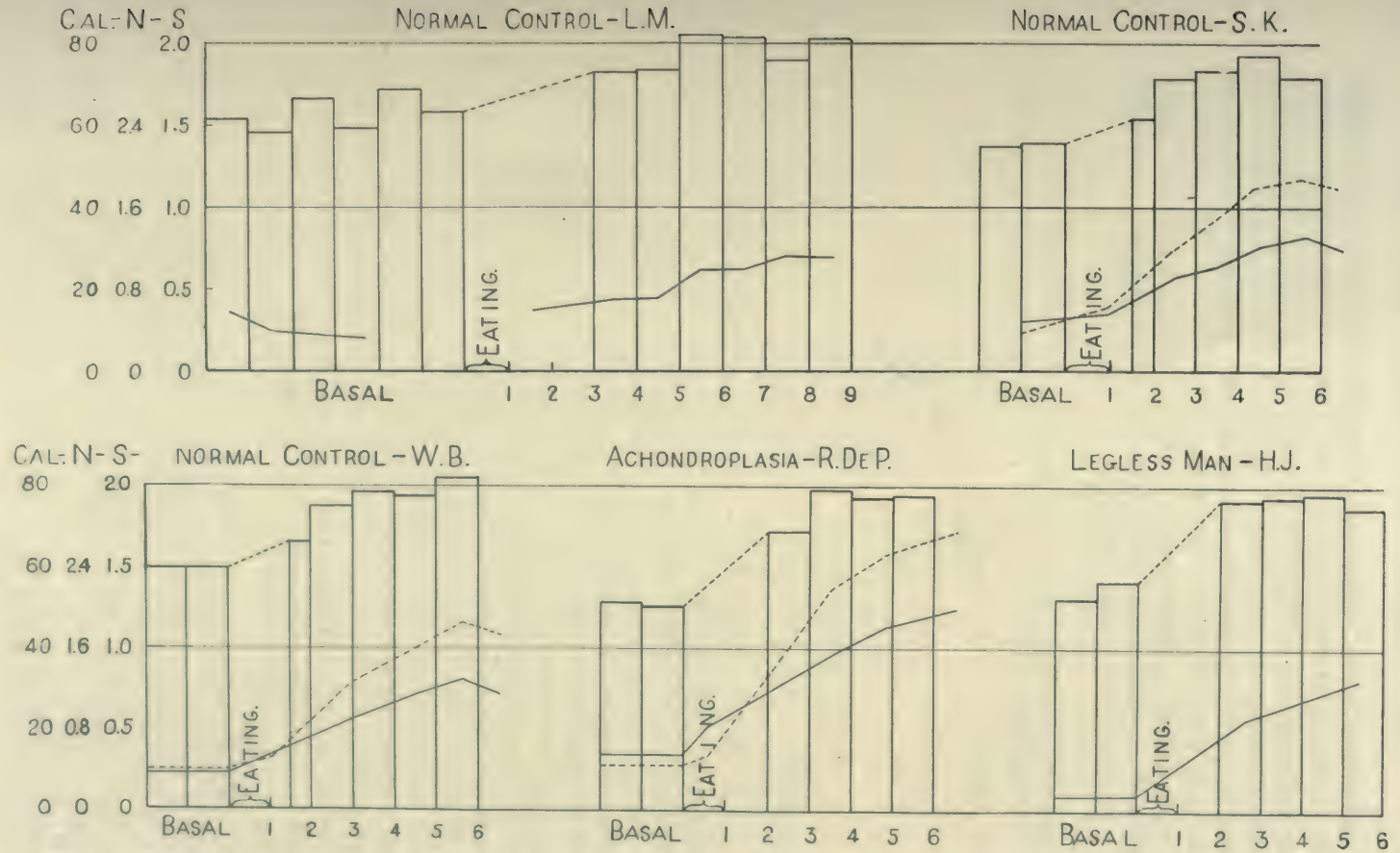

Chart 1.—Specific dynamic action of protein. Columns show the basal heat production in calories per hour and the increased metabolism after the subject has eaten chopped beef containing 23 to 25 gm. of nitrogen. The dotted line represents the excretion of sulphur in the urine in decigrams. The continued line gives the nitrogen elimination in grams.

The observations brought out several points of interest. The graphic chart shows that the metabolism had risen to a considerable degree one and one-half hours after the meal, and nearly to the maximum intensity two hours after eating. It remained at the high level for at least seven hours, with the maximum heat production between the fourth and sixth hours following ingestion of food. This shows that the absorption of food from the intestine is rapid, for certainly within one and one-half hours after partaking of food it has been partly absorbed from the bowel and is being metabolized.

TABLE 2.—NITROGEN AND SULPHUR EXCRETION IN THE DOG (AFTER RUBNER)

Period	Sulphur	Nitrogen	$\frac{N}{S}$
9-3	0.448	5.57	12.4
3-9	0.387	8.94	23.1
9-3	0.257	5.32	20.7
3-9	0.131	2.66	20.3

But what is the index of the true protein metabolism? Voit emphasized the fact that the amount of protein eaten was not good evidence of the amount metabolized, but that the urinary nitrogen was a much more direct index. But even though the urinary nitrogen is direct evidence, its hourly value is still rising for some hours after the stimulation of protoplasm has reached its maximum. This same fact has been observed in the study of dogs by Williams, Riche and Lusk,[20] who point out that there is a delay in the excretion of nitrogen following the metabolism of protein. They found that after giving 700 gm. of meat to the dog the maximum increase of metabolism was reached in two hours, but that the urinary nitrogen excretion did not reach its maximum until the sixth hour. There is, during this time, a temporary accumulation of nonprotein nitrogen, largely of the urea portion, in the blood and tissues, as was shown by Folin and Denis[21] and by Miss Wishart.[22] It was also shown by Reilly, Nolan and Lusk[23] that in a dog made diabetic with phlorhizin, the sugar derived from the

20. Williams, Riche and Lusk: Metabolism of the Dog Following the Ingestion of Meat in Large Quantities, Jour. Biol. Chem., 1912, **12,** 349.

21. Folin, Otto, and Denis, W.: Protein Metabolism from the Standpoint of Blood and Tissue Analysis, Jour. Biol. Chem., 1911-1912, **11,** 87.

22. Wishart, Mary: Animal Calorimetry, Paper IX. The Influence of Meat Ingestion on the Amino-Acid Content of Blood and Muscle, Jour. Biol Chem., 1915, **20,** 535.

23. Reilly, F. H., Nolan, F. W., and Lusk, G.: Phlorhizin Diabetes in Dogs, Am. Jour. Physiol., 1898, **1,** 395.

protein was excreted more rapidly than was the nitrogen. This is direct proof of the delayed excretion of nitrogen after its metabolism. Lusk[24] and Csonka[25] have shown that the administration of amino-acids to the phlorhizinized dog causes a maximal rise in both the heat production and sugar elimination in the first one or two hours, which indicates

TABLE 3.—NITROGEN-SULPHUR RATIOS AFTER MEAT INGESTION

Name	Date	Time	Nitrogen per Hour, Gm.	Sulphur per Hour, Mg.	$\frac{N}{S}$	Remarks
R. DeP.	3/15	7:20 a. m. to 1:10 p. m.	0.60	.....	....	Basal
	3/16	5:00 a. m. to 8:55 a. m.	0.57	31.9	17.7	662 gm. meat at 9:00 a. m.
		8:55 a. m. to 9:55 a. m.	0.87	35.3	24.7	
		9:55 a. m. to 12:17 p. m.	1.27	82.6	15.7	
		12:17 p. m. to 1:32 p. m.	1.61	135.6	11.9	
		1:32 p. m. to 3:04 p. m.	1.88	159.7	11.8	
		3:04 p. m. to 4:02 p. m.	2.02	173.0	11.7	
S. K.	5/16	9:27 a. m. to 1:26 p. m.	0.46	22.7	20.2	Basal
	5/18	9:15 a. m. to 11:23 a. m.	0.55	38.8	14.2	660 gm. meat at 8:20 a. m.
		11:23 a. m. to 12:22 p. m.	0.91	74.8	12.2	
		12:22 p. m. to 1:23 p. m.	1.02	94.1	10.9	
		1:23 p. m. to 2:32 p. m.	1.19	111.8	10.1	
		2:32 p. m. to 3:30 p. m.	1.29	117.9	10.9	
		3:30 p. m. to 4:24 p. m.	1.19	111.7	10.6	
W. B.	5/23	8:45 a. m. to 1:02 p. m.	0.37	25.0	14.6	Basal
	5/25	6:55 a. m. to 8:23 a. m.	0.54	32.7	16.6	600 gm. meat at 8:25 a. m.
		8:23 a. m. to 10:29 a. m.	0.61	34.4	17.7	
		10:29 a. m. to 12:30 p. m.	0.92	80.8	11.4	
		12:30 p. m. to 1:30 p. m.	1.12	104.3	10.7	
		1:30 p. m. to 2:28 p. m.	1.22	118.2	10.3	
		2:28 p. m. to 3:29 p. m.	1.13	110.7	10.2	
Harry J.	5/10	5:00 a. m. to 9:46 a. m.	0.38	25.7	14.7	660 gm. meat at 9:00 a. m.
		9:46 a. m. to 1:48 p. m.	0.94	61.1	15.3	
		1:48 p. m. to 3:07 p. m.	1.30	114.5	11.3	

that the rise in heat production approximately parallels the speed of amino-acid metabolism. This is before the period of maximal nitrogen elimination. Then, too, the sulphur portion of the protein is excreted

24. Lusk, G.: Animal Calorimetry, Paper XI. An Investigation Into the Causes of the Specific Dynamic Action of the Foodstuffs, Jour. Biol. Chem., 1915, **20,** 610.

25. Csonka, F. A.: Animal Calorimetry, Paper X. The Rate at Which Ingested Glycocoll and Alanine Are Metabolized, Jour. Biol. Chem., 1915, **20,** 539.

TABLE 4.—Data of Calorimeter—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 3 (Saml. G.)..	Prelim.	10:14	.....	.....	.....	.....	.....	.....	.....
3/8/16									
34.9 Kg.	1	10:50	13.4	11.9	0.82	19.2	0.261	39.6	40.2
1.08 Sq. M									
Case 4 (Pat W.)...	Prelim.	11:38	.....	.....	.....	.....	.....	.....	.....
3/24/16									
37.3 Kg.	1	12:38	15.7	13.7	0.83	16.1	0.266	46.0	47.1
1.20 Sq. M.									
	2	1:38	17.1	15.8	0.79	17.3	0.266	52.3	50.1
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Case 5 (Erwin E.).	Prelim.	12:05	.....	.....	.....	.....	.....	.....	.....
3/6/16									
37.4 Kg	1	1:05	12.1	10.6	0.83	12.5	0.314	35.3	40.6
1.17 Sq. M.									
	2	2:05	11.9	10.0	0.86	12.5	0.314	33.7	38.0
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
* Case 2 (Geo. F.)...	Prelim.	11:40	.....	.....	.....	.....	.....	.....	.....
1/7/16									
53.1 Kg.	1	12:40	16.4	14.0	0.86	16.5	0.309	47.0	51.8
1.51 Sq. M									
	2	1:40	16.2	15.0	0.79	16.2	0.309	49.6	50.6
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Case 8 (S. K.).....	Prelim.	10:50	.....	.....	.....	.....	.....	.....	.....
5/12/16									
50.4 Kg.	1*	11:20	11.5	9.6	0.87	13.0	1.288	31.7	32.5
1.50 Sq. M.									
	2	12:20	26.1	21.2	0.89	23.2	1.288	70.6	66.5
	3	1:20	25.3	22.1	0.83	27.4	1.288	72.3	71.8
	4†	2:30	28.9	25.9	0.81	35.5	1.288	84.4	89.1
	5‡	3:20	19.7	18.6	0.77	25.4	1.288	59.9	62.5
S. K.	Prelim.	10:56	.....	.....	.....	.....	.....	.....	.....
5/16/16									
49.5 Kg.	1	11:56	18.3	16.5	0.81	28.3	0.457	54.8	61.6
1.50 Sq. M.									
	2	12:56	17.9	16.9	0.77	26.1	0.457	55.5	61.2
	Aver.	.....	.....	.....	.....	.....	.....	....	.....
Case 7 (Robt. L.)..	Prelim.	11:21	.....	.....	.....	.....	.....	.....	.....
12/9/14									
63.8 Kg.	1	12:21	18.2	16.0	0.83	23.5	0.536	53.0	57.8
1.43 Sq. M.									
(measured)	2	1:21	21.1	19.0	0.81	24.9	0.536	63.0	65.3
	3	2:21	19.8	18.6	0.77	24.8	0.536	60.9	64.0
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Case 6 (Harry J.).	Prelim.	11:06	.....	.....	.....	.....	.....	.....	.....
12/11/14									
55.8 Kg.	1	12:06	20.7	18.8	0.80	23.7	0.419	62.5	59.3
1.33 Sq. M.									
	2	1:06	22.1	18.1	0.89	25.2	0.298	61.6	62.0
	3	2:06	21.9	19.9	0.80	24.5	0.298	66.2	61.3
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....

* 30-minute period. † 70-minute period. ‡ 50-minute period.

—Experiments in Dwarfs and Legless Men

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Lin.)	
.....	36.9	80	.....	.....	..	..	..	....	....	Basal; in bed
58.3	36.9	80	11	0.82	18	40	42	1.51	48.9	Quiet, 45 min. period; at 11:32 became nauseated
.....	36.6	....	.....	.....	..	..	..	....	....	Basal; in bed
46.9	36.6	70	15	0.84	15	48	37	....	....	Asleep 30 minutes; very quiet
50.9	36.6	79	17	0.79	14	63	23	....	....	Awake; quiet
.....	.....	....	.....	.....	15	55	30	1.32	41.0	
.....	37.3	....	.....	.....	..	..	..	....	....	Basal; in bed
35.0	37.2	61	11	0.84	..	..	..	....	....	Very quiet; asleep 30 min.; read 10 min.
35.3	37.1	64	7	0.88	..	..	..	....	....	Quiet; no reading
.....	.....	....	.....	0.86	24	36	40	0.92	29.5	
.....	37.0	....	.....	.....	..	..	..	....	....	Basal; in bed
47.1	36.9	59	15	0.87	17	37	46	....	....	Quiet; dozed
47.4	36.8	59	16	0.79	17	61	22	....	....	Quiet
.....	.....	....	.....	0.83	17	49	34	0.89	31.1	
.....	36.8	....	.....	.....	..	..	..	....	....	9:15 to 10:12, ate 662 gm. beef containing 24.1 gm. N.
29.9	36.7	67	4	0.95	54	8	38	....	....	Very quiet
66.8	36.7	....	12	0.99	48	2	50	....	....	Very quiet
69.5	36.7	69	18	0.86	47	25	28	....	....	Very quiet
88.3	36.7	69	26	0.82	47	32	21	....	....	Quiet
61.4	36.7	65	.....	0.74	48	46	6	....	....	Quiet
.....	36.4	....	.....	.....	..	..	..	....	....	Basal; in bed
53.9	36.2	55	3	0.81	..	..	..	....	....	Very quiet; almost motionless
70.9	36.2	55	9	0.76	..	..	..	....	....	Very quiet; urinated
.....	.....	....	.....	.....	22	57	21	1.11	36.8	
.....	36.9	....	.....	.....	..	..	..	....	....	Basal
51.7	36.8	78	8	0.84	27	40	33	....	....	Asleep
63.2	36.8	72	22	0.81	23	50	27	....	....	Fairly quiet
63.4	36.8	73	19	0.76	23	62	15	....	....	Fairly quiet
.....	.....	....	.....	.....	..	..	..	....	41.3	
.....	36.8	....	.....	.....	..	..	..	....	....	"Basal"
53.4	36.7	64	13	0.80	15	56	26	1.12	....	Restless
62.0	36.7	65	16	0.91	13	27	60	1.10	....	Restless
62.2	36.8	62	13	0.80	12	60	28	1.19	....	Restless

TABLE 4.—Data of Calorimeter Experiments—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Harry J.	Prelim.	10:36	.....	.....	.....	.....	.....	.....	.....
5/5/16									
54.6 Kg.	1	11:36	17.8	15.9	0.82	25.6	0.210	53.1	54.2
1.34 Sq. M.	2	12:36	18.5	17.4	0.78	24.8	0.210	57.5	55.0
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Harry J.	Prelim.	11:00	.....	.....	.....	.....	.....	.....	.....
5/10/16									
55.8 Kg.									
1.34 Sq. M.	1	12:00	26.2	23.9	0.80	28.9	1.298	77.9	69.3
	2	1:00	27.1	23.9	0.83	33.7	1.298	78.2	74.8
	3	2:00	27.8	24.0	0.84	40.6	1.298	78.9	81.3
	4	3:00	26.3	23.1	0.83	43.9	1.298	75.6	80.3
Case 1.....	Prelim.	11:02	.....	.....	.....	.....	.....	.....	.....
(Raphael DeP.)									
3/15/16	1§	12:05	18.9	16.8	0.82	22.5	0.603	52.8¶	54.0
40.9 Kg.									
1.24 Sq. M.	2‖	1:02	16.6	15.0	0.81	20.8	0.603	51.9¶	50.6
	3	.....	.....	.....	.....	.....	.....	.....	.....
Raphael DeP.	Prelim.	11:02	.....	.....	.....	.....	.....	.....	.....
3/16/16									
40.9 Kg.	1	12:02	24.6	21.6	0.83	27.8	1.27	70.8	63.7
1.24 Sq. M.							(1.88)**	(69.6)**	
	2	1:02	28.4	24.6	0.84	43.6	1.61	80.5	78.9
							(1.88)	(79.9)	
	3	2:02	27.1	24.2	0.82	50.6	1.75	78.2	82.6
							(1.88)	(77.9)	
	4	3:02	26.1	24.5	0.77	50.7	1.88	78.2	81.4
							(1.88)	(78.2)	
	5	4:02	.....	.....	.....	.....	2.02	.....	.....
Case 9 (G. T. B.)..	Prelim.	11:04	.....	.....	.....	.....	.....	.....	.....
5/23/16									
54.4 Kg.	1	12:04	20.8	18.3	0.83	29.5	0.380	61.1	60.6
1.56 Sq. M.	2	1:04	20.3	17.9	0.83	28.5	0.380	59.8	63.2
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
G. T. B.	Prelim.	9:55	.....	.....	.....	.....	.....	.....	.....
5/25/16									
55.5 Kg.	1	10:25††	12.4	9.9	0.91	22.6	1.219	33.7	33.3
1.56 Sq. M.	2	11:25	27.2	22.8	0.87	42.1	1.219	75.7	76.9
	3	12:25	27.4	24.0	0.83	40.4	1.219	79.0	75.7
	4	1:25	26.7	23.8	0.82	37.4	1.219	78.0	79.3
	5	2:25	27.9	24.9	0.81	40.6	1.219	81.7	84.5

** Figures in brackets based on assumption that the maximum nitrogen excretion represents true protein metabolism for whole experiment.
§ 63-minute period. ¶ Per hour. ‖ 57-minute period. †† 30-minute period

—IN DWARFS AND LEGLESS MEN—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Lin.)	
.....	.....	....	.....	.....	..	..	..	....	47.7	Excluded from averages on account of restlessness
.....	36.7	60	.....	.....	..	..	..	....	....	Basal; in bed
49.9	36.6	58	7	0.82	..	..	..	....	....	Very quiet; asleep 30 minutes
56.5	36.7	60	7	0.77	..	..	..	....	....	Very quiet
.....	.....	....	.....	0.79	10	63	27	1.01	41.3	
.....	36.9	....	78	.....	..	..	..	....	....	8:30 to 9:50 a. m. ate 660 gm. beef containing 24.6 gm. N.
68.5	36.9	14	76	0.79	44	40	16	....	58.1	Fairly quiet
76.3	36.9	16	83	0.85	44	29	27	....	58.4	Fairly quiet
84.9	37.0	22	84	0.88	44	24	32	....	59.0	Fairly quiet; voided
79.7	37.0	13	83	0.85	46	28	26	....	56.4	Quiet
.....	36.5	....	.....	.....	..	..	..	....	....	Basal
52.5	36.5	68	1	0.83	..	..	..	....	....	Awake; motionless
49.7	36.4	64	1	0.81	..	..	..	....	....	Awake; motionless
.....	.....	....	.....	0.82	31	43	26	1.28	42.2	9:00 to 10:05 a. m. ate 662 gm. beef containing 23.2 gm. N.
.....	36.9	....	.....	.....	..	..	..	....	....	
71.7	37.1	77	4	0.85 (0.88)**	47 (72)**	28 (11)**	25 (17)**	1.72 (1.69)	57.1 (56.1)	Asleep 60 minutes. Motionless
78.8	37.2	83	12	0.88 (0.90)	53 (63)	19 (12)	28 (25)	1.96 (1.94)	65.0 (64.5)	Awake; very quiet
81.6	37.2	84	12	0.83 (0.84)	59 (64)	23 (20)	18 (16)	1.90 (1 89)	63.0 (62.8)	Awake; very quiet
78.1	37.1	79	10	0.72 (0.72)	64 (64)	34 (34)	2 (2)	1.90 (1.90)	63.0 (63.0)	Awake; very quiet
.....	36.8	....	.....	.....	..	..	..	....	....	Basal; normal control
63.9	36.9	58	6	0.83	..	..	..	....	....	Almost motionless
63.3	36.9	58	8	0.83	..	..	..	....	....	Almost motionless
.....	.....	....	.....	.....	17	47	36	1.11	38.7	8:30 to 9:15 a. m. ate 600 gm. beef containing 23.7 gm. N.
.....	36.9	....	.....	.....	..	..	..	....	....	
34.0	36.9	60	0	0.94	24	15	61	....	....	Motionless
75.4	37.0	66	12	0.92	43	17	40	....	....	Almost motionless
80.3	37.1	54	17	0.85	41	30	29	....	....	Almost motionless
77.5	37.1	64	17	0.82	42	35	23	....	....	Almost motionless
85.2	37.1	72	17	0.82	40	37	23	....	....	Almost motionless

more rapidly than the nitrogen, as first shown in dogs by Rubner[26] and in humans by Wolf.[27] Rubner's figures were taken in six-hour periods and show how long continued is the high nitrogen excretion after a meat diet containing 24.7 gm. nitrogen.

The sulphur elimination is shown in Table 2 to be very much more rapid. One would expect the nitrogen to sulphur ratio to be 16, which is that found in meat, but because of the variation in speed of excretion, the ratio falls during the first six hours and is too high in the following periods.

Our observations, which are made in very much shorter periods and extend only to seven hours after food, confirm these findings, except that in the hour during the ingestion of food the nitrogen excretion rises markedly; the sulphur increases but little. This is probably due to the rapid elimination of the extractives in the meat.

This delayed elimination of nitrogen after marked protein ingestion makes its hourly excretion a poor index of the metabolism during that hour. Since the total metabolism stays at a nearly constant level throughout the observation after food, it seems probable that the protein metabolism also stays at a constant level. The same value ought, therefore to be used throughout the observation, not a different one for each hour. The best value to use seems to be the maximum hourly nitrogen excretion and this has been used in all calculations. The effect of this choice is but slight in regard to the height of the total hourly metabolism, but the percentage of calories derived from the three foodstuffs is markedly affected, particularly in the early hours of the observation. This effect can be seen in Table 4, in which, in the case of R. De P., the calculations are made in both ways: (1), using the N as excreted; and (2), using the maximum value as the hourly excretion. The figures for Louis M. will be found in Paper 4 of this series.

The tables show quite clearly that no matter which value is assumed as the true protein metabolism, in the first hours of the observation a large part of the specific dynamic action is at the expense of the oxidation of carbohydrates. This is true of all cases except that of Louis M., in whom the 100 gm. of fat taken with the meat probably affected the relationship. This finding is not in accord with the results of Gigon.[28] He used casein and found that the specific dynamic action was due to protein metabolism alone, and that carbohydrate and fat were even spared slightly. Gigon's results on the increased heat production fol-

26. Rubner, Max: Die Gesetze des Energieverbrauchs bei der Ernährung, Leipzig, 1902, p. 369.

27. Wolf, C. G. L.: Die Ausscheidungszeit von Stickstoff, Schwefel und Kohlenstoff nach Aufnahme von Eiweisssubstanzen und Spaltungsprodukten, Biochem. Ztschr., 1912, **40,** 234; ibid., 1912, **41,** 111.

28. Gigon, A.: Ueber den Einfluss der Nahrungsaufnahme auf den Gaswechsel, Arch. f. Physiol., 1911, **140,** 509.

lowing casein ingestion are of interest in relation to the percentage increase which we have found. The results obtained by Gigon were recalculated by Williams, Riche and Lusk,[20] and the chart of their findings is here reproduced (Table 5). It shows an average specific dynamic action (70) which is lower than that reported in this paper (76). This difference is possibly due to the different form of protein ingested.

Staehelin[29] obtained, in one observation, results which are quite different from those of Gigon or from those here reported. He used a Jaquet apparatus, determining the metabolism in two hourly periods. The test meal consisted of 75 gm. of protein and 12.2 gm. of fat. In the twelve-hour observation following the meal the urine nitrogen increased 0.37 gm. per hour, which represents 9.9 calories of increased protein metabolism. The respiratory observation, however, indicates

TABLE 5.—Increase of Metabolism in Man Due to Protein Ingestion (Gigon)

Food Casein, Gm.	Increase in Protein Metabolism		Increase in Total Calories of Metabolism	100 Calories of Protein Metabolism Increases Total Calories by
	Gm.	Calories		
50	7.1	28.4	19	67
100	23.8	95.2	53	56
150	35.7	142.8	118	83
200	58.1	232.4	171	74
Average				70

an average increased elimination by the body of 24.6 calories per hour and an increase in the proportion of fat metabolized. This result is not in accord with the other experiments here recorded.

Another conclusion may be drawn from the observations as viewed in Table 6. The relationship between the normal and abnormal cases shows that the specific dynamic action did not follow the surface area. The three normal cases have values per square meter which are very close together. The percentage increase of the two abnormal cases, however, is distinctly higher, which shows that diminishing the surface area or muscle volume did not proportionally reduce the intensity of the specific dynamic action. In the last column of the chart is shown the total percentage increase, found by dividing the actual increase in metabolism by the calories of extra protein oxidized. If one allows for the increased heat due to the fat ingestion of Louis M., the ratios

29. Staehelin, R.: Versuche ueber Gaswechsel und Energieverbrauch nach Nahrungsaufnahme, Ztschr. f. klin. Med., 1908, **66**, 201.

are all closely related. We interpret this to mean that the specific dynamic action is dependent in these cases on the total protein metabolism. It is certainly independent of the mass of muscle tissue.

NORMAL CONTROLS

In the course of these experiments and of those recorded in Paper 20 of this series there have been six basal observations on normal men between the ages of 23 and 34. Four are new subjects whose metabolism has not been previously determined.

The basal metabolism of E. F. D. B. was determined four times in the spring of 1913, when an average value of 39.8 calories per square meter per hour was found. In May, 1915, the metabolism by the same index was 37.6 calories. In May, 1916, the height of his metabolism was 38.4 calories. This shows the constancy of the basal metabolism of some normal individuals.

TABLE 6.—SPECIFIC DYNAMIC ACTION. PERCENTAGE INCREASE

Name	Physical Condition	Urinary Nitrogen		Calories Extra Protein Metabolized per Hr. Extra N × 26.5	Actual Calories Increase per Sq. M. per Hr.	100 Calories of Protein Metabolism Increases Cals. per Sq. M. by	Actual Total Calories Increase per Hr.	100 Calories of Protein Metabolism increases Total Calories by
		Basal, per Hr.	After Meat, per Hr.					
R. DeP.	Achondroplasia	0.60	1.88	33.9	19.4	57.2	24.1	71.1
Harry J.	Legless man	0.21	1.30	28.9	16.6	57.5	22.3	77.2
Louis M.*	Normal control	0.52	1.14	16.4	8.3	50.5	15.3	93.1*
W. B.	Normal control	0.38	1.22	22.3	11.7	52.6	18.2	81.8
S. K.	Normal control	0.46	1.29	22.0	11.1	50.5	16.6	75.5

* Regular protein meal plus 100 gm. of fat.

The metabolism of J. H. M. had been determined by the Benedict unit apparatus and reported in the series of Palmer, Means and Gamble,[30] and of Means.[2] The average of these observations is 39.4 calories per square meter per hour. These findings were made more than a year before our determination (39.5 calories) and on a different type of apparatus.

The average calories per square meter per hour of these six controls is 38.9. The average found in this laboratory for normal men between the ages of 20 and 50 is 39.7 calories per square meter per hour. The six controls reported here average 2 per cent. below this figure (Table 7).

30. Palmer, W. W., Means, J. H., and Gamble, J. L.: Basal Metabolism and Creatinin Elimination, Jour. Biol Chem., 1914, **19**, 239.

TABLE 7.—Summary of Basal Metabolism of Six Normal Controls. Men

Name	Date	Age	Height, Cm.	Weight	Surface Area, Sq. M. Linear Formula	Calories per Sq. M. per Hour	Variations from Average Normal 39.7 %	Average R. Q.	Total Calories Measured		Divergence of Direct from Indirect, per Cent.
									Indirect	Direct	
E. F. D B.	4/12/16	34	179.5	76.47	1.94	38.8	—2.2	0.80	150.71	161.79	+7.4
	4/25/16*	..	.....	.....	1.95	37.6	—5.4	0.80	73.23	71.54	—2.3
J. H. M.	4/21/16	30	177.0	75.34	1.89	39.5	—0.6	0.80	149.12	155.04	+4.0
J. C. F.	4/27/16	23	178.0	64.29	1.75	41.7	+5.1	0.82	146.05	149.18	+2.2
J. C. A.	4/29/16	26	175.2	60.20	1.64	39.2	—1.3	0.86	128.46	149.49	+16.3
S. K.	5/16/16	33	161.5	49.53	1.50	36 8	—7.4	0.79	110.31	114.84	+4.1
G. T. B.	5/23/16	25	164.5	54.37	1.56	38.7	—2.4	0.83	120.87	127.17	+5.2
Average	.....	..	.....	.....	....	38.7	—2.4	....	.....	.....	+5.7

* One hour experiment. All others two hours.

SUMMARY

1. The basal metabolism of five dwarfs, two legless men and six normal controls is reported. The legless men and the dwarfs, with apparently normal endocrine systems, showed, in relation to their surface area, the same level of metabolism as normal men. The law of surface area holds good for men of unusual body shape.

2. The dwarfs with involvement of the ductless glands and symptoms of cretinism showed a marked reduction in metabolism below the average found in normal cases, as has been reported by other authorities.

3. Following the ingestion of large quantities of meat, the excretion of urinary nitrogen during the earlier hours is not an accurate index of the protein metabolism. The sulphur excretion is more rapid than the nitrogen excretion.

4. The stimulation of metabolism following a large amount of meat is almost at its height two hours after the meal is eaten. The extra heat produced may amount to three-quarters of the calories in the protein metabolized, and may lead to an increase of 46 per cent. above the level of the basal heat production.

5. The specific dynamic action of a meal containing 24 gm. of nitrogen in the form of meat was larger in the case of a legless man, and of an achondroplastic dwarf, with very small arms and legs and normal trunk, than in the cases of three normal controls of greater weight and greater surface area. This indicates that the intensity of the specific dynamic action is not proportional to the mass of the musculature. The true explanation of the results cannot be given in the light of present knowledge. Various possible explanations come naturally to mind, such, for example, as a greater concentration of amino-acids in the blood flowing to the muscles, or the presence of a liver, which, in proportion to the size of the organism, is relatively larger than the normal.

477 First Avenue.

CLINICAL CALORIMETRY

TWENTY-SECOND PAPER

THE RESPIRATORY METABOLISM IN NEPHRITIS*

JOSEPH C. AUB, M.D., AND EUGENE F. DU BOIS, M.D.
WITH THE TECHNICAL ASSISTANCE OF G. F. SODERSTROM
NEW YORK

A study of the syndrome known as *nephritis* should throw a great deal of light on many problems of normal and pathologic physiology. The disease is accompanied by profound changes of long duration, and the organism is obliged to adapt itself to conditions which are very different from those found in health. For this reason the investigator can obtain in the study of nephritis much information as to the manner in which the total metabolism is influenced by certain factors. Chief among these are nitrogen retention, edema, high blood pressure, acidosis and the conditions which cause uremia. Unfortunately, we know little about these factors, and suspect the presence of many more about which we know nothing. At this stage, all that one can do is to present his findings as completely as possible in the hope that they will be of service to those who can some day solve the nephritis problem. In the meantime, the study will help in the solution of many related questions.

The basal metabolism of patients with cardiac and renal disease was discussed briefly in Paper 16 of this series. The literature was reviewed and the results obtained on sixteen patients were published in such detail as was possible. Some of these patients had been studied in the early days of the calorimeter, before the general recognition of the importance of many of the modern measurements and tests. In most of the patients studied the cardiac element predominated, but in about half there was an important nephritic element also. It was found that the total metabolism of patients with mild cardiac or renal disease was normal, and that five of the twelve patients with dyspnea showed an increase in metabolism of 25 to 50 per cent. The respiratory quotients were all within normal limits and the method of direct calorimetry gave results only 1.9 per cent. lower than the method of indirect calorimetry. No direct relationship was found between the level of the metabolism and the acidosis, height of blood pressure or the ability of the kidney to excrete phenolsulphonephthalein. In

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* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division, Bellevue Hospital.

Table 2 of Paper 16 the results of the clinical and laboratory findings were compared.

This present work is a continuation of Paper 16 and Tables 2 and 3 have been made to correspond as closely as possible with Table 2 of the previous publication. More attention has been given to blood analyses, the methods for estimating the degree of acidosis, and the functional capacity of the kidneys. The patients were all primarily nephritics and were selected from a large number in the effort to obtain young people with few complications. For the first time since the calorimeter work was begun, patients with an absolutely bad prognosis were used as subjects.

METHODS

The men patients were studied in the metabolism ward and calorimeter fully described in previous papers. The two women patients could not be brought to the metabolism ward, and it was impossible to study their intake and output, but otherwise they were treated in just the same manner as the men. Patients with orthopnea were placed in the steamer chair while in the calorimeter; all others used the bed, with head rest and pillow. Most of the patients were given a cup of "caffein-free" coffee (Kaffee Hag) without cream or sugar, early in the morning of the experiment. Except for this they were all fasting, having received no food since the previous afternoon. While in the apparatus they were all quiet, except the uremic patients, Isadore R. and Frank C.

The blood pressure was measured by the Faught apparatus, diastolic readings being made at the diminution of the murmur in the artery, which usually occurs just before its disappearance. The phenolsulphonephthalein test of Rowntree and Geraghty was used, the results in the tables being expressed as the total excretion in two hours and ten minutes. The carbon dioxid combining capacity of the plasma was determined by the Van Slyke method.

The blood and urinalyses, while the patients were in the metabolism ward, were made by Dr. Frank C. Gephart of the staff of the Russell Sage Institute of Pathology. While the patients were in the general medical wards the analyses were made, for the most part, in the Pathological Department of Bellevue Hospital by Drs. A. O. Gettler and Willis Baker. To them and to Dr. Norris we are indebted for permission to publish the results. These authors have recently published a valuable contribution on the "Chemical and Physical Analysis of Blood in Thirty Normal Cases."[1]

DISCUSSION OF RESULTS

The manifestations of nephritis are so varied that it will require the study of many cases to give all the information that is needed. Nevertheless, much can be learned from the ten cases summarized in Table 2 and the sixteen cases of the previous publication. (See Table 2, Paper 16).

Direct and Indirect Calorimetry.—In the thirteen[2] experiments here reported the total calories, as measured by the method of indirect

1. Gettler, A. O., and Baker, Willis: Jour. Biol. Chem., 1916, **25,** 211.
2. The experiment on Mildred C. is omitted because the direct method could not be used.

calorimetry, was 1,700.4; by the method of direct calorimetry, 1,743.3, or 2.5 per cent. higher. In the previous work, the calories by the indirect method totaled 4,297.7, and by the direct method, 4,214.5, which was 1.9 per cent. lower. These two divergences of the direct calorimetry almost neutralize each other, and in the grand total of all the work the indirect is 5,998.1; the direct, 5,957.8, which is 0.7 per cent. lower. This agreement is just as close as in the case of a group of normal controls, and it shows that the calorific value of one liter of oxygen is the same in nephritics and normals. We must not forget, however, that there may be striking changes in the intermediary metabolism without great change in the calorific value of oxygen. This is brought out clearly in the work on diabetes.

Respiratory Quotients.—Except in the cases of diabetes and in convalescence, the respiratory quotient fourteen hours after the last meal is little more than the expression of the amount of carbohydrate available in the organism. This depends on the state of nourishment, the amount of carbohydrate food taken the preceding day, and the level of the total metabolism which determines the rate at which this carbohydrate is oxidized. Nephritic patients, as a rule, are given carbohydrate diets unless the total calories are greatly restricted. It is not surprising, therefore, that quotients as high as 0.93 and 0.89 were found. On the other hand, the lowest quotients obtained, 0.77 and 0.78, are well within normal limits. This confirms the statement made a year ago that there is no need to assume any change in the type of the metabolism from the normal.

Total Metabolism.—The calculations of the total metabolism are based on the measurements obtained by the method of indirect calorimetry and are expressed as calories per square meter of surface per hour. This figure is then compared with the standard average normal figure for the same age and sex, as given in Table 7 of Paper 13 of this series, and the percentage variation from the normal recorded. Most of the subjects could be compared with the group of normal men between the ages of 20 and 50, the average calories per square meter per hour being 39.7. The results obtained on John C., 62 years old, were compared with the figure 37, which is about the average for his time of life according to the revised curve given in Paper 19. This makes him 10 per cent. above the normal. He still had his youthful vigor, and it is well to remember that his metabolism was only 3 per cent. above the standard for men 20 to 50 years of age. Edna S. presents a different problem. She was only 13 years old, and the standard for girls of this age is 47 calories per square meter per hour. For two months before the calorimeter observation she had been on a restricted

diet, and this may reduce the metabolism even more in a child than in an adult. Direct evidence on this point is lacking, but it can be seen in Table 9 of Paper 17 that the four children with severe diabetes show an unusual reduction in metabolism. The observation on Frank C., with uremia, was almost spoiled by his restlessness, which was even greater than is indicated by the high work-adder. The results were 29 per cent. above the basal standard, but those who observed him were confident that his muscular activity alone could have increased his metabolism 20 to 30 per cent., and it is doubtful if his basal metabolism would have been higher than the average normal. It is unfortunate that the otherwise satisfactory experiment on Mildred C. should be marred by the possibility that she had exophthalmic goiter. Her nervous temperament and exophthalmos, which was greater than is generally found in nephritis, suggested this factor.

A. Influence of Dyspnea.—Isidore R., Frank C., and John C. were distinctly dyspneic, and they all showed a slight increase in metabolism. This increase was not as marked as in the four out of five patients with moderately severe dyspnea described in the paper on cardiacs and nephritics.

B. Acidosis.—According to the carbon dioxid combining capacity of the plasma, a rather severe type of acidosis was present in the case of Joseph U. on April 5, and in Isidore R. on January 24. The former showed a metabolism of 7 per cent. below the normal; the latter, only 2 per cent. above. Slight acidosis was found in Joseph U. on April 10, and in Jack K. on March 4. Their figures were —12 per cent. and +5 per cent., respectively. These results, taken with the figures obtained in Papers 16 and 17, indicate that acidosis has little effect on the total metabolism.

C. Edema.—There was marked edema in the cases of Joseph U., Lee H., Edna S. and William S. The first three showed a distinct reduction in metabolism. With Adam P., January 14, the edema was moderate and the metabolism 10 per cent. below the average normal. In general, the type of nephritis with edema is accompanied by a reduction in metabolism; the type without edema, by a slight increase in metabolism. One naturally expects an organism diluted by inert fluid to show a diminished metabolism according to body weight. Obesity patients have such a reduction, but Means has proved that they have the same metabolism per square meter of surface as normal people.[3]

3. Means, J. H.: Studies of the Basal Metabolism in Obesity and Pituitary Disease, Jour. Med. Research, 1915, **32,** 121; The Basal Metabolism in Obesity, THE ARCHIVES INT. MED., 1916, **17,** 704.

Edematous cardiac patients as a rule show an increased metabolism, but here other factors may be involved. The reduction of metabolism per square meter of surface found in nephritic edema is sometimes very marked (—27 and —40 per cent.), and it points to some cause other than mere dilution of tissue and distention of skin.

D. High Blood Pressure.—All the patients except Lee H. showed a rise in blood pressure. The systolic pressure was above 200 mm. in the cases of Adam P., January 14, Isidore R., Frank C., John C. and Mildred C. Of these, Adam P. showed a reduced metabolism and the others an increase. With Adam P. the metabolism was about the same when his systolic pressure was 185 mm. as when it was 230 mm. George M., of Paper 16, showed exactly the same figures for a blood pressure of 160 mm. as for a pressure of 195 mm. On the other hand, Joseph U. showed a drop in metabolism when his blood pressure fell. Blood pressure has no constant influence on the total metabolism.

E. Eliminative Power of the Kidney.—Curiously enough, most of the patients were able to eliminate at least 6 gm. of nitrogen in the urine on the calorimeter days, and Lee H. was the only one, except the incontinent patients, Isadore R. and Frank C., in whom the urine volume was much diminished. On the other hand, the chlorid elimination was low in most of the patients, probably on account of the low intake in some cases, but in most on account of inability on the part of the kidney to excrete salt. The phthalein output was low in all cases except Joseph U. on April 5, and Lee H. on December 4. The Ambard coefficient expressed in terms of the McLean index was low in the cases of Joseph U. and Frank C.

The nonprotein nitrogen was above the normal limits in the cases of Joseph U., Jack K., Isidore R., Frank C.; and the urea nitrogen was above normal in Lee H. also. One of these patients showed a decrease in metabolism, the others a slight increase. In general, it does not seem that the products retained by damaged kidneys have any direct effect on the level of the total metabolism.

CHANGES IN INDIVIDUAL CASES

Joseph U. was in the calorimeter three times, and during the whole period there was little change in the McLean index and blood urea. In the first experiment his metabolism was higher than normal. In the next week he lost 5 kg. of edema and his metabolism fell to 7 per cent. below the normal average. At this time he had a distinct acidosis and furnished an excellent opportunity to study the effect of this factor on metabolism. Accordingly, he was given sodium bicarbonate until the acidosis almost disappeared and there was scarcely any change in his metabolism.

Lee H. was studied, December 4, and again a month later, when he had gained 5.5 kg. of edema. During this same period there was a marked fall in the phthalein output and increase in the retention of urea and creatinin. His metabolism in the first test had been 12 per cent. below the average normal; a month later it was 27 per cent. below. Part of this decrease was undoubtedly due to rest and low diet.

Adam P. was in the calorimeter January 14 and again three and a half weeks later, when he had lost 8 kg. of edema. In this interval there was practically no change in the phthalein excretion or in the blood urea, but the blood pressure fell 45 mm. There was hardly any alteration in the level of his total metabolism.

SUMMARY AND CONCLUSIONS

Ten patients with nephritis were studied in the calorimeter. All were severe cases, and it was possible to examine five of the patients shortly before death. The results have been compared with those obtained last year on a series of patients with cardiorenal disease, six of whom were primarily nephritics.

In the present series nine experiments were made on edematous subjects. All but two of these tests showed a diminution of the basal metabolism, both according to body weight and to surface area. In two cases with great edema the heat production was 27 and 40 per cent. below the normal average.

Five patients suffering from nephritis of the chronic interstitial type, without edema, were studied. One with marked uremia was at the normal level of metabolism. Another, who was very restless, showed an increase. A third, in whom hyperthyroidism was suspected, also showed an increase. The other two were near the upper normal level of metabolism.

In most of the patients with greatly increased blood pressure the metabolism was higher than in the other nephritics with lower blood pressures. Most of the patients with marked dyspnea showed some increase in metabolism. No relationship could be established between the level of metabolism and the degree of acidosis or the eliminative power of the kidney, as estimated by the McLean index, the phenolsulphonephthalein test, the elimination of salt and nitrogen, and the analysis of the various substances in the blood, such as chlorids, urea, and the nonprotein nitrogen.

The methods of direct and indirect calorimetry in this and the previous series of cardionephritics give totals which agree within 0.7 per cent. The respiratory quotients are all within normal limits, showing that nephritics derive their energy from very much the same proportions of the various foodstuffs as do normal men.

The normal quotients found in patients with low carbon dioxid com-

bining capacity of the plasma prove that nephritic acidosis is not caused by difficulty in oxidizing carbohydrates.

Edematous nephritics kept on low diets show a reduction in food requirement similar to that usually found in prolonged undernutrition. Other nephritics have approximately the normal food requirement.[4]

CASE HISTORIES

CASE 1.—Joseph U., aged 19; chronic parenchymatous nephritis with acute exacerbation. Admitted March 27, 1916; died April 23, 1916.

History.—Five years prior to the test he had scarlet fever. Recently he has been a sign painter's helper but has not been much exposed to the danger of lead poisoning. His habits are good. For several years he has passed his water once or twice during the night. Early in March, 1916, after a wetting, he noticed edema of the eyelids, then edema of the ankles, disappearing at night. About March 20 the edema of the legs became permanent and a few days before admission the genitalia became edematous. He feels perfectly well.

Physical Examination.—Height 175 cm.; well nourished; color pasty; marked edema of face, back, genitalia, thighs and legs. Heart: Apex beat in the fifth space 11.5 cm. to the left of the median line. Left limit of dulness 12.5 cm. to the left; right limit, 3 cm. to the right of median line. Sounds are of good quality; no murmurs. Lungs are clear. There is marked acne of face and back.

The clinical data are given in Table 4 and a summary of the more important findings in Tables 2 and 3. His urine contained a large amount of albumin, pus casts and many granular casts; no glucose. The McLean indexes were as follows: March 31, 49; April 4, 46; April 10, 39. The CO_2 combining power of the plasma was as follows: April 4, 39 volume per cent.; April 5, 39 per cent.; April 8, 40 to 50 per cent.; April 9, 60 per cent.; April 10, 55 per cent.; April 16, 39 per cent.; April 19, 48 per cent.

Calorimeter observations were made on March 29, April 5 and April 10. From March 29 to April 10 he was on a mixed diet containing about 1,500 calories, 5 gm. nitrogen and 1.5 gm. salt, with about 1,500 c.c. fluids in addition to the water of the so-called solid foods. He was given hot air baths almost every day, responding unusually well, losing between 480 and 900 gm. weight during the baths. His temperature was normal, he felt well and he lost 5 kg. weight in twelve days, the edema almost disappearing. During this period he passed 1,000 to 1,500 c.c. urine a day, containing from 10 to 13 gm. of nitrogen and 2 to 5 gm. of chlorids. The prognosis would have been favorable were it not for the low phthalein output on two occasions, the low McLean index, the high nonprotein nitrogen and high urea of the blood and the low carbon dioxid combining power of the plasma. The high phthalein output of April 4 stood in contrast to the other tests.

In order to eliminate the factor of acidosis he was given 40 gm. sodium bicarbonate between 6 p. m., April 8 and 6 p. m., April 9, the two days before the last calorimeter test.

On April 11 the picture changed markedly. He became very weak in the hot air bath and was removed at once. The temperature rose to 105 F. and remained elevated for five days. During this period his pulse was 98 to 124; respiration, 24 to 40. The edema increased. On the day after the onset,

4. The above work is a continuation of studies in cardiac and renal disease carried on a year previously in association with Dr. Francis W. Peabody of Boston. It is a pleasure to record the active participation of Dr. Peabody in about half of the experiments of this present series.

TABLE 1.—Nephritis. Data of—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 1 (Joseph U.) 3/29/16	Prelim.	11:48	.....	.....	.....	.....	.....	.....	.....
75.7 Kg. 1.84 Sq. M.	1	12:48	26.6	25.2	0.77	34.6	0.555	82.9	88.0
	2	1:58	26.8	25.1	0.78	35.5	0.555	82.9	86.9
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Joseph U. 4/5/16	Prelim.	.....	.....	.....	.....	.....	.....	.....	.....
70.8 Kg. 1.83 Sq. M.	1	11:58	22.6	22.6	0.73	28.8	0.375	73.9	77.2
	2	12:58	23.3	19.5	0.87	28.5	0.375	65.9	77.5
	3	1:58	22.7	18.3	0.90	28.5	0.375	62.5	78.0
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Joseph U. 4/10/16	Prelim.	.....	.....	.....	.....	.....	.....	.....	.....
70.6 Kg. 1.83 Sq. M.	1	12:27	23.6	21.2	0.81	22.5	0.408	70.7	74.2
	2	1:27	22.0	20.7	0.77	21.6	0.408	68.4	70.6
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Case 2 (Lee H.).... 12/4/15	Prelim.	11:00	.....	.....	.....	.....	.....	.....	.....
55.1 Kg. 1.57 Sq. M.	1	11:57½	17.4	15.1	0.84	21.9	0.249	50.7	54.6
	2	1:00	19.7	17.1	0.84	26.0	0.249	57.7	61.7
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Lee H. 1/5/16	Prelim.	.....	.....	.....	.....	.....	.....	.....	.....
61.6 Kg. 1.70 Sq. M.	1	12:40	16.0	13.7	0.85	20.3	0.296	46.1	51.1
	2	1:41	17.5	16.1	0.79	22.5	0.296	53.4	57.2
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Case 3 (Edna S.).. 12/1/15	Prelim.	.....	.....	.....	.....	.....	.....	.....	.....
48.2 Kg. 1.39 Sq. M.	1	12:39	14.2	11.0	0.94	18.0	0.713	38.1	40.0
	2	1:39	14.6	11.9	0.89	17.7	0.713	40.7	40.9
	3	2:09	7.2	5.4	0.96	8.6	0.713	18.9	20.7
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Case 4 (Adam P.) 1/14/16	Prelim.	.....	.....	.....	.....	.....	.....	.....	.....
60.5 Kg. 1.60 Sq. M.	1	12:25	19.1	17.0	0.82	22.1	0.340	56.6	61.2
	2	1:25	19.0	17.6	0.79	21.6	0.340	58.3	62.8
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Adam P. 2/7/16	Prelim.	.....	.....	.....	.....	.....	.....	.....	.....
52.5 Kg. 1.52 Sq. M.	1	12:30	17.5	16.4	0.78	21.9	0.163	54.5	55.7
	2	1:30	17.1	14.8	0.84	21.3	0.163	50.0	54.1
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Case 10..... (Isidore R.) 1/24/16	Prelim.	11:58	.....	.....	.....	.....	.....	.....	.....
63.2 Kg. 1.87 Sq. M.	1	12:28	13.0	11.9	0.79	17.9	.....	39.6	43.3
	2	12:58	13.8	13.8	0.73	19.5	.....	45.2	45.0
	3	1:28	11.8	9.5	0.90	15.6	.....	32.7	34.1
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....

—Calorimeter Experiments

Direct Calorimetry, Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Lin.)	
.....	37.1	....	.....	.....	..	..	..	....	....	Basal; in bed
84.4	37.1	66	19.0	0.76	..	..	..	....	....	Quiet; reading 15 minutes
81.2	37.0	66	19.0	0.77	..	..	..	....	....	Quiet; not reading
.....	.....	....	.....	.....	18	66	16	1.10	45.1	
.....	36.9	....	.....	.....	..	..	..	....	....	Basal; in bed
66.2	36.7	55	16.0	0.72	..	..	..	....	....	Quiet
79.6	36.7	55	5.0	0.88	..	..	..	....	....	Very quiet
73.6	36.7	55	15.5	0.92	..	..	..	....	....	Very quiet
.....	.....	....	.....	.....	15	66	19	0.95	36.9	
.....	36.9	....	.....	.....	..	..	..	....	....	Basal; in bed
74.0	36.9	63	12.0	0.81	..	..	..	....	....	Quiet; asleep 15 minutes
85.9	37.2	64	4.0	0.77	..	..	..	....	....	Motionless
.....	.....	....	.....	.....	16	61	23	0.99	38.0	
...	36.6	48			..	..	..	....	....	Basal; in chair
48.4	36.5	44	15.0	0.84	..	..	..	....	....	Fairly quiet; dozed
54.1	36.4	44	15.0	0.84	..	..	..	....	....	Fairly quiet
.....	.....	....	.....	.....	12	44	44	0.98	34.5	(1st period–57½ min. (2d period–62½ min.
.....	36.8	61	.....	.....	..	..	..	....	....	Basal; in bed
54.9	36.9	67	10.0	0.86	17	41	42	....	....	Very quiet
52.4	36.8	68	14.0	0.79	15	62	23	....	....	Very quiet, until end of period; 61 minute period
.....	.....	....	.....	...	..	..	..	0.80	29.0	
... ..	37.0	....	.....	. .. .	..	..	..	....	....	Basal; in chair
37.3	37.0	82	1.0	0.94	..	..	..	....	....	Very quiet; reading
40.7	37.0	83	2.4	0.90	..	..	..	....	....	Very quiet
21.8	37.0	80	1.5	0.97	..	..	..	....	....	Very quiet; reading; 30 minute period
.....	.....	....	.....	.....	5	21	74	0.81	28	
.....	37.2									
55.9	37.1	58	6.0	0.82	16	52	32	....	....	Very quiet
58.0	37.0	59	25.0	0.78	16	63	21	....	....	Somewhat restless
.....	.....	....	.....	.....	..	..	..	0.95	35.9	
.....	36.9	....	.....	.....	..	..	..	....	....	Basal; in bed
53.3	36.9	60	13.0	0.77	8	71	21	....	....	Very quiet
49.6	36.8	53	15.0	0.84	9	50	41	....	....	Quiet
.....	.....	....	.....	.....	..	..	..	1.00	34.4	
.....	37.1-	....	.....	.....	..	..	..	....	....	"Basal"; in bed; irrational
41.0	37.0	92	23.0	.....	..	..	..	....	....	Fairly restless; 30 min. period
44.3	37.0	96	30.0	.....	..	..	..	....	....	Restless; 30 min. period
38.2	37.1	....	6.0	.....	..	..	..	....	....	Asleep; very quiet; 30 min. period
.....	.....	....	.....	.....	..	..	..	1.24	41.9*	

* Results closer to true basal figures are obtained by using average R. Q. and taking CO_2 figures for first and third periods. This gives an average of 40.4 calories per square meter per hour.

TABLE 1.—Nephritis. Data of—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 5 (Jack K.)... 3/4/16	Prelim.	11:58	.....	.....	.....	.....	.....	.....	.....
58.3 Kg.	1	12:58	24.7	20.1	0.89	23.3	0.525	68.2	69.0
1.62 Sq. M.	2	1:58	23.9	19.6	0.89	25.1	0.525	66.3	75.1
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Case 6 (Frank C.) 2/28/16	Prelim.	11:46	.....	.....	.....	.....	.....	.....	.....
Missing	1	12:44	23.2	23.4	0.72	21.1	0.525	.....	67.4
1.54 Sq. M.	2	1:21	18.1	14.2	0.92	16.0	0.525	.....	47.8
	Total 95 min.	.....	.....	.....	.....	.....	.....	124.8	
	Aver. per hr.	.....	.....	.....	.....	.....	.....	78.9	.....
Case 7 (John C.).. 2/9/16	Prelim.	.....	.....	.....	.....	.....	.....	.....	.....
69.8 Kg.	1	12:40	24.3	23.9	0.74	32.3	0.276	78.4	81.7
1.87 Sq. M.	2	1:40	25.0	22.1	0.82	30.9	0.276	74.3	79.9
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Case 8..... (Mildred C.)	Prelim.	11:57	.....	.....	.....	.....	.....	.....	.....
12/10/16	1	12:57	19.9	16.6	0.87	21.6	0.231	.....	49.7
49.7 Kg.	2	1:57	21.4	23.1	0.68	31.6	0.231	.....	61.9
1.40 Sq. M.	Aver.	.....	.....	.....	.....	.....	.....	65.8	.....
Case 9 (Wm. S.)... 12/6/16	Prelim.	11:40	.....	.....	.....	.....	.....	.....	.....
64.2 Kg.	1	12:40	22.2	20.9	0.77	26.1	0.483	68.8	68.3
1.66 Sq. M.	2	1:40	22.4	20.6	0.79	27.5	0.483	68.3	70.5
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....

bronchial voice and breathing were heard over the right lower lobe. Two days later there was a small area of dulness and bronchial breathing at the angle of the left scapula. April 16 the temperature was normal and the patient felt weak but much better. By the 19th he was drowsy and his respirations slow and deep. There was persistent flatness and diminished breathing over the right lower lobe, but only 2 c.c. cloudy, sterile fluid could be withdrawn by needle. On the afternoon of the 22d he suddenly began to have violent convulsions, lasting until his death, shortly after midnight. No necropsy could be obtained.

After the febrile attack, which was probably pneumonia, the urine volume diminished rapidly, with a marked fall in the output of nitrogen and salt. This was in part due to a diarrhea.

Case 2.—Lee H., aged 21, Chinaman, cook; chronic parenchymatous nephritis with acute exacerbation. Admitted Nov. 19, 1915, died Jan. 14, 1916.

History.—It was impossible to get any information as to the character of his previous illnesses. He says that he has always been well. He has been in New York five years. He says his present trouble began about Nov. 1, 1915.

Physical Examination.—Height 170 cm.; frame small, whole body, including face and scalp, markedly edematous. His color is pasty; he is orthopneic and dyspneic. Heart: Apex beat in the fifth space 10 cm. from median line; no murmurs. Lungs: At both bases, flatness, diminished breath sounds and

—CALORIMETER EXPERIMENTS—(*Continued*)

Direct Calorimetry, Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Lin.)	
.....	36.9	72			..	..	..	....	....	Very quiet; basal Asleep 35 min.
63.4	36.8	60	5.0	0.92	..	..	..	....	....	Reading 10 min.
68.0	36.7	68	13.5	0.92	..	..	..	....	....	Very quiet; awake
.....	.....	....	.....	.....	21	23	56	1.2	41.5	
.....	37.0	88	.....	.....	..	..	..	....	....	Basal (restless)
71.0	37.1	86	47.0	.....	..	..	..	....	....	58 min. period; very restless
50.6	37.2	89	54.0	.....	..	..	..	....	....	37 min. period; very restless
76.8	.....	....	.....	0.80	18	57	25	1.6	51.2	Very unsatisfactory observation
.....	37.2	63								
74.9	37.1	57	19.0	0.74	..	..	..	....	....	Very quiet
75.5	37.1	60	18.5	0.83	..	..	..	....	....	Quiet
.....	.....	....	.....	0.78	10	68	22	1.1	40.8	
.....	.....	104	.....	.....	..	..	..	....	....	Basal; in chair
.....	.....	103	5.0	0.88	..	..	..	....	....	Very quiet; slept
.....	.....	104	11.0	0.66						
.....	.....	....	.....	0.77	9	73	18	1.32	47.0	Rectal thermometer out of order
.....	38.1	85								
74.9	38.3	86	6.0	0.76	..	..	..	....	....	Quiet
71.1	38.3	83	5.0	0.79	..	..	..	....	....	Quiet
.....	.....	....	.....	.....	19	62	19	1.07	41.2	

fremitus. Radial arteries slightly thickened. Eyegrounds normal. Abdomen contains some fluid.

Patient was in the calorimeter December 4 and January 5. For clinical data December 4 and January 5 to 12, see Table 6, and also the summary, Tables 2 and 3.

The urine contained a large amount of albumin and many hyaline and granular casts. The specific gravity was high, usually in the neighborhood of 1.040. Glucose was absent. On some examinations red blood cells were found in the urine. The Wassermann test was faintly positive on three examinations. November 24 the blood urea was 32 mg.; creatinin, 0.84 mg.; chlorids, 0.51 mg.; freezing point, —0.647 C.; December 4, alveolar CO_2 38 mm. Hg; January 4, blood urea was 49 mg.; ammonia nitrogen, 1.1 mg.; chlorids, 0.612 per cent.; creatinin, 3.9 mg.; CO_2 combining capacity, 70 per cent. The phenolsulphonephthalein excretion in two hours was as follows: December 3, 64 per cent.; December 18, 44 per cent.; January 12, 13 per cent.

The blood pressure was not increased: Systolic, 115 to 120 mm.; diastolic, 75 to 85 mm.

The patient was kept on a moderately restricted diet and was given hot packs. His edema continued to increase but the dyspnea and orthopnea were not distressing and the patient remained cheerful. The physical signs of fluid in the pleural cavities and abdomen were practically unchanged.

January 4 he began to have fever in the afternoons, reaching 101 to 103 F., with morning remissions. He complained of pain in the abdomen and chest and began to cough. Over the lungs, anteriorly, there developed many moist, crackling râles, and over the precordium a cardiorespiratory friction rub. The urine volume fell to 600 to 900 c.c., with 11 to 17 gm. nitrogen and only a trace of chlorids. His bowels moved four to seven times a day. The patient grew more toxic and dyspneic but had no convulsions. He died, January 13. Postmortem aspiration of the pleural cavities and abdomen yielded milky fluid containing very few cells, but many diplococci. There was no necropsy.

The blood on January 7 showed hemoglobin, 75 per cent.; red blood cells, 4,500,000; leukocytes, 10,000; no filaria.

Case 3.—Edna S., aged 13, schoolgirl, born in New York. Admitted Oct. 7, 1915; died May 2, 1916; chronic parenchymatous nephritis with acute exacerbation.

History.—Previous history negative except for measles and a mild sore throat. In 1912 she had a cough for a month and went to a physician who said she had kidney trouble. For the previous two years she had had frequent nosebleeds, but no frequency of micturition, headache, dizziness or edema until the present trouble. Sept. 1, 1915, her mother noticed edema of the face. October 4 she was put to bed by the family physician on account of edema of the legs. October 6 she lost her vision and had a convulsion of the right side of the body, and was also in a convulsion when she was brought to the hospital the next day.

Physical Examination.—Color pasty; face, body and extremities very edematous. The patient is a well nourished, intelligent girl, orthopneic and slightly dyspneic. Respirations, Cheyne-Stokes. Tonsils large, with deep crypts. Heart: Left border of dulness in the fifth space 2 cm. to the left of the midclavicular line; right border 2 cm. to the right of the midsternal line. The second sound in the aortic area is markedly accentuated; no murmurs. The liver edge is felt 2 cm. below the free margin of the ribs. The fundi of the eyes show slight haziness of the disk outlines. The blood pressure, which was 160 mm., dropped to 115 mm. after removal of 350 c.c. blood from vein.

On repeated examinations the urine showed large amounts of albumin, many hyaline and granular casts, and sometimes red blood cells. It was acid, contained no glucose, and the specific gravity averaged about 1.020.

The patient was given a restricted diet, with fruit and plenty of carbohydrate, but very little nitrogen and only small amounts of fluid. She was also given a daily hot pack. November 15 and again March 3 she had convulsions during which venesections were performed. In November and December there was little change in her general condition, the edema being extreme and the urine volume always scanty. The patient was in the calorimeter December 1.

January 28 fluid began to collect in the left pleural cavity. April 18 the temperature, which had been normal, rose to 101 F., then became very irregular, reaching 106 F., April 29. Cough and pain in the chest developed. She became more and more toxic and stuporous and died May 2, 1916. No necropsy could be obtained.

The phthalein tests were as follows: November 15, 16 per cent.; November 23, 61 per cent.

The blood tests: November 15: urea nitrogen, 14.5 mg.; November 18: urea nitrogen, 22.6 mg.; November 30: nonprotein nitrogen, 18.9 mg.; March 3: total nonprotein nitrogen, 19.7 mg.; urea nitrogen, 16.2 mg.; blood CO_2 combining power, 62 volume per cent.

The spinal fluid, March 3, removed when the patient was stuporous, ten minutes before the convulsions began, was under increased pressure.

Case 4.—Adam P., aged 26, Russian, a tailor. Admitted Jan. 10, 1915; discharged improved, May 5, 1916; chronic parenchymatous nephritis with acute exacerbation.

History.—His father was a heavy drinker. At the age of 15 the patient had rheumatic fever for two months, involving many joints. Since then he has had some subacute symptoms. Six months prior to the test he had tonsillitis. He uses beer in moderation.

About April, 1915, he noticed edema of the legs, which has gradually increased and has involved abdomen, arms and face. Shortly afterward, he began to suffer from dimness of vision, dizziness and headaches. He has had increasing nocturia and now passes urine three to four times at night.

Physical Examination.—A well developed young man with marked generalized edema. He is not dyspneic. Heart: Left border of dulness 12.5 cm. from the median line. The second pulmonic sound is accentuated. At the bases of the lungs there is some dulness and diminution of breath sounds. Eyes: Fundi show chorioretinitis of long duration. He can distinguish fingers only at a distance of 2 feet. Dr. Rees believes that the eye condition has nothing to do with the nephritis.

The urine contained a large amount of albumin and many hyaline and granular casts. The specific gravity varied between 1.016 and 1.025. On admission the blood analysis was as follows:

Sugar	90 mg.
Urea nitrogen	34.3 mg.
Ammonia nitrogen	0.25 mg.
Creatinin	0.5 mg.
Uric acid	3.7 mg.
Plasma chlorids	0.60 per cent.

The phthalein test in two hours was 27 per cent. and the McLean index was 67.

The blood pressure was about 200 mm. systolic and 130 mm. diastolic until February 3; then it fell to about 160-105 mm.

The patient was given a restricted diet and, at first, hot packs. The generalized edema and hydrothorax continued. He was in the calorimeter January 14. At this time there were about 10 kg. of retained fluid in the edema. The daily urine volume was 1,000 to 1,500 c.c.; urine nitrogen, 8 to 11 gm.; chlorids, 5 to 8 gm. The patient lost weight steadily and when next in the calorimeter, February 7, had almost no edema. The McLean index February 8, was 25. The output of water, nitrogen and chlorids in the urine exceeded the intake. The calories in the diet were just about sufficient to cover the requirement. The volume per cent. of CO_2 in the plasma was as follows: January 13, 58; January 18, 62; February 8, 66.

The patient continued to improve slowly and by March 5 had no edema and no dyspnea and was able to get out of bed for a few hours. He was still unable to distinguish fingers at a greater distance than 4 feet. March 5, after walking a few steps, he complained of pain in the back. The next day the urine contained blood. For the following week he had pain over the right kidney, slight fever, many pus cells and a few red blood cells in the urine. The Roentgen ray revealed no calculus. Infarction of the kidney was suspected.

The pus in the urine disappeared in a few weeks. On March 17 the urine culture showed streptococci. He grew stronger and on May 5 was sent to a convalescent home. While on measured diets several experiments were made to determine the effect of sodium bicarbonate on his weight and the carbon dioxid combining capacity of his plasma.

Case 9.—William S., aged 27, laborer, was admitted to the Fourth Medical Division, service of Dr. Nammack, Nov. 16, 1915; discharged improved Feb. 4, 1916; chronic parenchymatous nephritis.

History.—At the age of 9 he had scarlet fever, followed by impairment of the hearing. Two years prior to the test he had urethritis. During the previous year the legs and ankles were swollen at intervals and the face and genitalia were at times edematous. Recently, he has had headaches and pain in the back and lower thoracic region. He has had no dyspnea or cyanosis.

TABLE 2.—Nephritis. Summary—

Case Number and Name	Date in Cal'r.	Age, Yrs.	Diagnosis	Status	Temp., C.
1. Joseph U.	3/29	19	Chronic parenchymatous, Ac. Exac.	Died 4/23	37.1
	4/ 5	..	.....	.....	36.7
	4/10	..	.....	.....	37.0
2. Lee H.	12/ 4	21	Chronic parenchymatous, Ac. Exac.	Died 1/14	36.5
	1/ 5	..	.....	.....	36.8
3. Edna S.	12/ 1	13	Chronic parenchymatous, Ac. Exac.	Died 5/2	37.0
4. Adam P.	1/14	26	Chronic parenchymatous, Ac. Exac.	Improved	37.1
	2/ 7	..	.....	.....	36.8
9. William S.	12/ 6	27	Chronic parenchymatous	Improved	38.3
5. Jack K.	4/ 4	28	Chronic interstitial	Improved	36.8
10. Isidore R.	1/24	26	Chronic interstitial, uremia	Died 1/27	37.1
6. Frank C.	2/28	19	Chronic interstitial, uremia	Died 3/27	37.1
7. John C.	2/ 9	61	Chronic interstitial	Improved	37.1
8. Mildred C.	12/10	39	Chronic interstitial (hyperthyroidism?)	Improved	....

TABLE 3.—Nephritis. Summary—

Case Number and Name	Date in Cal'r.	Urine				Ambard McLean Index	Blood	
		24 Hr. Volume, C.c.	Total N, Gm.	Total Cl as NaCl	Phthalein per Cent. in 2 Hrs.		Nonprotein N, Mg.	Urea, Mg.
1. Joseph U.	3/29	1,520	12.1	4.1	10	48	—	59.5
	4/ 5	946	9.1	1.8	79	47	100.0	57.4
	4/10	935	9.3	2.3	16	39	117.0	53.2
2. Lee H.	12/ 4	570	7.2	—	64	..	.....	32.0
	1/ 5	260	7.8	0.9	13	..	.....	49.0
3. Edna S.	12/ 1	.....	....	...	..	..	.....	....
4. Adam P.	1/14	1,280	7.7	4.8	27	67	39.4	20.5
	2/ 7	1,340	6.7	4.1	31	..	41.0	18.9
9. William S.	12/ 6	1,230	10.7	—	48	..	41.7	17.3
5. Jack K.	3/ 4	1,750	6.8	6.9	8	82	72.5	53.9
10. Isidore R.	1/24	.....	....	...	..	..	165.0	58.1
6. Frank C.	2/28	.....	....	...	18	49	49.7	18.9
7. John C.[4]	2/ 9	975	8.1	5.8	35	..	33.3	16.1
8. Mildred C.	12/10	.....	....	...	20	134	26.2	13.2

1. On November 24.
2. Below 47, the normal for a girl of this age.
3. Very restless.
4. 62 years old.

—OF CLINICAL DATA

Pulse	Resp. Rate	Dyspnea	Orthopnea	Periodic Resp.	Cyanosis	Edema	Blood Pressure, Syst.	Blood Pressure, Diast.
66	.....	±	—	—	—	++	175	108
55	.....	—	—	—	—	+	144	84
64	.....	±	—	—	—	+	150	94
46	15-18	+	+	—	—	+	110	80
67	.....	+	+	—	—	++	115	85
82	.....	±	++	—	—	+++	148	105
59	.....	—	—	—	—	Mod.	230	140
57	.....	—	—	—	—	—	185	120
85	20-25	±	±	..	—	++	178	90
65	.....	—	—	—	—	—	197	145
94	.....	++	—	++	±	—	155	100
88	.....	+++	++	+	..	—	220	145
60	.....	+++	++	++	+	—	230	125
104	.....	+	+	..	——	—	260	170

—OF LABORATORY DATA

Blood			CO_2 Comb. Power, Volume per Cent.	Calories per Sq. M. per Hour	Variation from Average Normal Lin.	Calories per Kg.	R. Q.
Creatinin, Mg.	Total Chlorids, Mg.	CO_2 Comb. Power, Mm. Hg.					
....	0.649	..	....	45.1	+14	1.10	0.77
1.91	0.665	26	38.8	36.9	— 7	0.95	0.83
....	0.634	38	55.0	38.0	— 4	0.99	0.79
0.84[1]	0.51 [1]	47	....	34.5	—13	1.00	0.84
3.9	0.612	..	70.2	29.0	—27	0.80	0.82
....	.....	..	....	28.0	—40[2]	0.81	0.93
....	0.623	..	57.8	35.9	—10	0.95	0.80
....	0.672	..	66.3	34.4	—13	1.00	0.81
....	.....	31[5]	....	41.2	+ 4	1.07	0.78
2.6	0.740	35	52.8	41.5	+ 5	1.15	0.89
....	0.609	19[6]	43.6	40.4[7]	+ 2	....	0.82[8]
....	0.528	..	63.5	51.2[8]	+29	1.56	0.82
....	0.594	..	69.1	40.8	+10	1.09	0.78
....	0.694	..	....	47.0	+27	1.32	0.77

5. Alveolar air.
6. On January 21
7. Calculated from CO_2 of first and third periods.
8. Somewhat restless throughout.

Physical Examination.—A somewhat undernourished young man with marked edema of the whole body, including face and genitalia. The heart is enlarged, the left border of dulness being 12.5 cm. to the left of the median line; the right border, 6 cm. to the right. At the bases of the lungs there is dulness and diminished resonance and breath sounds. There is some fluid in the abdomen.

The urine was acid; specific gravity 1.018 to 1.022; glucose absent; albumin present in large amounts, with many hyaline and granular casts and many red blood cells. Wassermann weakly positive.

December 3, a note says: "Patient lying flat in bed in no distress. Hands are blue; face neither cyanotic nor edematous. Heart sounds of good quality; no murmurs. Second sound is reduplicated; second aortic sound much accentuated. Lungs: Dulness at bases extends on both sides to within three finger-breadths of scapulae. There are a few coarse râles at the left base. Abdomen much distended and dull in right flank. No shifting dulness or fluid wave. There is marked edema of body wall from costal margin downward, and of legs and feet, and slight edema of thighs and genitalia." The phthalein test was 48 per cent. December 3. Blood pressure: 160 mm. systolic; 95 mm. diastolic. Patient was in the calorimeter December 6.

December 6, before he was put in the calorimeter, the temperature began to rise and continued irregular, reaching 103 F.; pulse 74 to 100; respirations 18 to 28. The patient developed a cough and the lungs showed many râles but no consolidation. December 8 the alveolar CO_2 was 31 mm. Hg. December 13 the febrile attack ended and patient improved steadily, but on February 4, when he was discharged, he still complained of swelling of the ankles and slight headache. The table of clinical data (Table 6), December 4 to 6, shows the urine volume 800 to 1,300 c.c., with 8 to 11 gm. nitrogen.

Case 5.—Jack K., aged 28, baker. Admitted Feb. 15, 1916; discharged improved; chronic interstitial nephritis.

History.—At the age of 7 the patient had diphtheria. In 1901, while in the army, he had malaria. He has had frequent sore throats and in 1912 had rheumatic fever following tonsillitis. The same year he had urethritis. He was formerly a heavy drinker.

In August, 1914, he began to have pain in the head and lumbar region, epistaxis, vomiting, dizziness, edema of legs, weakness and frequency of urination. He was in the hospital for a long time, being discharged only two months before entrance into Bellevue. Feb. 12, 1916, he had nosebleed, occipital headache and dizziness. Things got black before his eyes. February 15, the day of admission, he noticed edema of the legs. He has been passing urine three to five times at night and has lost 8 pounds in one month. He has had no night sweats or cough.

Physical Examination.—A well developed and well nourished man of rather sullen demeanor. He is not dyspneic or cyanotic and there is only slight edema of the feet. Heart: Left border of dulness in the fifth space is 12.5 cm. from the median line; right border, 4 cm. to the right of median line. Radial arteries are hardened. Lungs are clear. Eyes: Fundi show slight haziness of disk outline and of vessels.

March 4 the patient was in the calorimeter. His condition was practically unchanged except that the edema had disappeared.

His urine was acid; specific gravity 1.010 to 1.012 on repeated examinations and in two-hour day and night specimens. Glucose was absent. Albumin was present in a heavy cloud, with casts, a few leukocytes, but no red blood cells. The Wassermann test on the blood was negative.

The blood pressure was, systolic, between 214 and 197; diastolic, between 96 and 145.

Phthalein Tests: February 19, 13 per cent.; March 3, 8 per cent.

Blood: February 23, nonprotein nitrogen 90.7 mg. March 3, nonprotein nitrogen 72.5 mg.; urea nitrogen, 53.9 mg.; creatinin, 2.6 mg.; chlorids, 0.740 per cent.; McLean index, 82. March 2, CO_2 combining capacity of plasma, 53 Vols. per cent.

CASE 10.—Isidore R., aged 26, pedler, Austrian Hebrew. Admitted Jan. 15, 1916; died Jan. 27, 1916; chronic interstitial nephritis; uremia.

History.—At the age of 9 years the patient had pneumonia; at 22 years, urethritis. In April, 1915, following exposure, he noticed swelling of ankles and face. Two months later the abdomen became swollen and he had anorexia and gastric distress. He went to the Michael Reese Hospital in Chicago, where he was told his blood pressure was 160 mm. He was treated with hot air baths, the ascites disappeared, and he was discharged in three months. Three weeks later the symptoms returned and he entered Mount Sinai Hospital, New York, where he was told his blood pressure was 200 to 210 mm. He left early in December and on December 21 entered Bellevue. Here his phthalein excretion, December 29, was 10 per cent. in two hours. He was transferred to the Metropolitan Hospital, but left after a few days. Previous to his second admission to Bellevue, Jan. 15, 1916, he suffered from dyspnea, edema, headache, oliguria, nausea and vomiting. The cause of his frequent changes of hospital was evidently his restless, insubordinate disposition.

Physical Examination.—January 20: A well nourished man in great distress; very pale; lying on two pillows, gasping for air, with marked sighing, deep respirations every five or six breaths. His mucous membranes were pale, his tongue coated, his pupils large and reacting sluggishly to light. Heart: Left border of dulness in the fifth space 1 cm. outside the nipple line; right border, 3 cm. from median line. The sounds are very short and snapping, with a true gallop rhythm. The lungs are clear. The abdomen is tense and tympanitic, with no dulness and no tenderness. There is no edema. The fundi show an albuminuric retinitis.

The urine, January 17, was acid; specific gravity 1.018; no glucose; albumin present in large amount; no casts seen and no red blood cells. January 19 the CO_2 combining capacity of the plasma was, in terms of alveolar CO_2, only 17 mm. Hg; January 21, only 19 mm. Since he refused all medication by mouth, he was given intravenously 400 c.c. of a 5 per cent. solution of sodium bicarbonate at 8 p. m., January 21. Half an hour later he had a chill and the pulse became very rapid. Next day the respirations, which had been rapid, shallow and periodic, became normal. The CO_2 capacity rose to 37 mm. Hg. He was brighter mentally, though still apathetic. A marked diarrhea developed. On the 23d, a pericardial rub was heard and the patient became more stuporous. He was in the calorimeter January 24. On the 27th he died. No necropsy could be obtained.

January 15 to 19 the temperature was 99 to 101; pulse 88 to 96; respirations 20 to 24; stools, one a day. January 20 to 27 the temperature was 100 to 101; pulse 92 to 110; respirations 12 to 36; stools, five to ten a day. The blood examinations were as follows:

January 20, nonprotein nitrogen, 103 mg.; chlorids 0.609 per cent. January 22, nonprotein nitrogen, 101 mg.; chlorids, 0.572 per cent. January 24, nonprotein nitrogen, 165 mg.; urea nitrogen, 68 mg.; chlorids, 0.609 per cent.

The CO_2 combining capacity of the blood plasma in volumes per cent. was as follows: January 19, 25; January 20, 29; January 21, 28; January 22, 55; (after bicarbonate) January 23, 53; January 24, 44; January 26, 51; January 27, 44.

The systolic and diastolic blood pressures were:

	Systolic, Mm.	Diastolic, Mm.
January 18	210	110
January 21	183	110
January 22	153	88
January 23	158	116
January 24	155	100

The patient took very small amounts of food and was incontinent so much of the time that it was impossible to collect twenty-four-hour specimens of urine.

TABLE 4.—NEPHRITIS—

Case Number Name and Date	Temperature Max.	Temperature Min.	Food Total Calories	Food Carbohydrate, Gm.	Food Fat, Gm.	Food N., Gm.	Urine N., Gm.	Excreta N.,[1] Gm.
Case 1 Joseph U. 3/29/16	99.4	97.8	1,081	145	42	3.9	12.1	12.5
3/30/16	99.0	97.4	1,287	176	49	4.4	11.1	11.6
3/31/16	98.8	97.8	1,551	225	54	4.9	13.2	13.7
4/ 1/16	Normal		1,554	215	59	5.0	11.3	11.8
4/ 2/16	Normal		1,553	213	59	5.2	11.4	11.9
4/ 3/16	Normal		1,579	216	61	5.1	9.6	11.1
4/ 4/16	Normal		1,455	207	52	4.8	9.7	10.1
4/ 5/16	Normal		1,200	164	53	5.4	9.1	9.6
4/ 6/16	Normal		1,712	226	64	7.4	9.8	10.5
4/ 7/16	Normal		1,474	207	54	4.9	9.5	10.0
4/ 8/16	98.6	97.0	1,673	228	56	5.0	9.2	9.7
4/ 9/16	Normal		1,433	197	55	5.0	9.3	9.8
4/10/16	Normal		1,375	186	51	5.2	9.3	9.9
4/11/16	105.0	99.4	1,252	182	42	4.4	11.2	11.6
4/12/16	104.8	100.4	0[2]	0	0	0	7.8[3]	7.8
4/13/16	102.8	99.6	609	31	45	2.6	4.7[4]	5.0
4/14/16	103.8	100.6	0[2]	0	0	0	2.4[5]	2.4
4/15/16	101.4	98.8	672	61	38	2.8	1.1	2.4
4/16/16	Normal		916	116	40	2.7	2.0	2.3
4/17/16	Normal		830	88	42	3.3	2.6	2.9
4/18/16	Normal		930	88	49	4.3	2.8	3.2
4/19/16	Normal		908	117	38	2.9	3.2	3.5
4/20/16	Normal		692	132	13	1.2	6.5	6.6
4/21/16	Normal		916	149	27	2.1	6.5	6.7
Case 6 Frank C. 2/27/16	Normal		989	124	43	3.2	15.6	15.9
2/28/16	Normal		664	60	39	2.1	11.9	12.2
3/24/16	Normal		1,687	250	60	4.2	17.5	17.9
3/25/16	Normal		792	108	32	1.8	15.7	15.9

1. Excreta nitrogen calculated as urine nitrogen plus 10 per cent. of food nitrogen.
2. Vomited.
3. 26 hours 20 minutes.
4. 21 hours 40 minutes.
5. 24 hours 10 minutes.

—Clinical Data

Nitrogen Balance, Gm.	Body Weight, Kg.	Urine Volume, C.c.	Calories per Kg.	Fluid Intake, C.c.	NaCl Intake, Gm.	Urine NaCl, Gm.	Blood Pressure, Syst.	Blood Pressure, Diast.
—8.6	75.7	1,520	14	1,020	1.34	4.08	175	108
—7.1	74.7	1,470	16	1,235	1.10	4.78	165	113
—8.8	73.5	1,682	21	1,470	1.44	4.91	168	110
—6.8	72.9	1,340	21	1,470	1.27	3.84		
—6.7	72.1	1,230	21	1,420	1.39	3.36		
—6.1	71.2	1,090	22	2,050	1.34	3.17		
—5.4	71.4	1,030	20	1,970	1.69	2.19		
—4.3	70.8	946	17	1,380	2.09	1.84	144	84
—3.1	71.4	1,056	24	1,680	2.09	2.03		
—5.0	71.8	995	20	1,400	1.31	1.66		
—4.7	70.8	1,000	23	1,725	1.77	1.66		
—4.8	71.3	1,040	20	2,020	1.74	1.84		
—4.6	70.6	935	19	2,150	1.97	2.30		
—7.2	72.1	1,090	17	2,875	1.38	1.18	150	94
—7.8	....	750[3]	0	1,360	0	0.52		
—2.4	71.2	480[4]	8	1,380	0.88	0.52	134	90
—2.4	....	250[5]	0	2,275	0	0.09		
+0.4	....	160	9	1,000	0.85	0.22		
+0.4	....	290	13	820	0.92	0.40	150	90
+0.4	71.0	350	11	1,005	1.02	0.40		
+1.1	71.0	360	12	1,515	1.54	0.26		
+0.5	70.9	420	12	1,200	1.05	0.31		
—5.4	71.1	400	9	760	0.52	0.45		
—4.6	70.9	380	12	950	0.77	0.36		
—12.7	51.0	2,340	19	2,010	....	4.03	220	145
—10.0	50.2	2,292	13	2,360	0.70	1.86		
—13.7	49.4	4,260	34	1,090	1.18	7.72		
—14.1	48.7	2,930	16	3,270	0.43	4.82		

TABLE 5.—NEPHRITIS.

Case Number, Name and Date	Food			Food N., Gm.	Urine N., Gm.	Excreta N.,[1] Gm.	Nitrogen Balance, Gm.
	Total Calories	Carbohydrate, Gm.	Fat, Gm.				
Case 4 Adam P.[2]	.....	...	..	...	....	....	.....
1/13/16	1,603	183	79	4.6	11.0	11.5	—6.9
1/14/16	1,606	148	95	4.6	7.7	8.2	—3.6
1/15/16	1,627	203	72	5.0	9.3	9.8	—4.8
1/16/16	1,609	203	72	4.4	8.1	8.5	—4.1
1/22/16	1,174	154	47	4.1	7.6	8.0	—4.0
1/23/16	1,464	204	53	5.2	8.2	8.7	—3.5
1/24/16	1,345	175	53	5.1	7.2	7.7	—2.6
1/25/16	1,616	224	61	5.1	7.7	8.2	—3.1
1/26/16	1,595	205	60	5.5	7.9	8.4	—2.9
1/27/16	1,391	186	54	5.0	6.6	7.1	—1.1
1/28/16	1,486	214	51	5.3	6.9	7.4	—2.1
1/29/16	1,434	179	62	4.8	6.0	6.5	—1.7
1/30/16	1,577	226	57	4.6	7.0	7.5	—2.9
1/31/16	1,601	216	63	5.3	7.9	8.4	—3.2
2/ 1/16	1,423	204	52	4.2	6.4	6.8	—2.6
2/ 2/16	1,518	202	60	5.0	6.2	6.7	—2.7
2/ 3/16	1,634	225	63	4.9	6.7[3]	7.2	—2.3
2/ 4/16	1,488	211	54	4.8	6.5[4]	7.0	—2.2
2/ 5/16	1,569	225	56	4.9	5.6[5]	6.1	—1.2
2/ 6/16	1,477	194	60	4.9	6.7[6]	7.2	—2.3
2/ 7/16	1,321	181	48	5.2	6.7	7.2	—2.0
2/ 8/16	1,558	221	56	4.8	6.6	7.0	—2.2
2/ 9/16	1,529	212	57	4.8	6.5	7.0	—2.1
2/10/16	2,153	195	103	15.2	7.0	8.5	+6.7
2/11/16	2,138	192	105	14.6	10.4	11.9	+2.7
2/12/16	2,024	204	87	14.9	11.1[7]	12.6	+2.3
2/13/16	2,029	199	86	15.1	12.2[8]	13.7	+1.4
2/14/16	2,010	191	90	15.2	13.7	15.1	+0.1

1. Excreta nitrogen calculated as urine nitrogen plus 10 per cent. of food nitrogen.
2. Temperature normal.
3. 25 hours 15 minutes.
4. 22 hours 25 minutes.
5. 23 hours 25 minutes.
6. 24 hours 55 minutes.
7. 22 hours 20 minutes.
8. 25 hours 35 minutes.

—Clinical Data

Body Weight, Kg.	Urine Volume, C.c.	Calories per Kg.	Fluid Intake, C.c.	NaCl Intake, Gm.	Urine NaCl, Gm.	Blood Pressure Syst.	Blood Pressure Diast.
.....	.....	..	.....	....	....	230	140
61.4	1,590	26	.....	2.57	7.48	226	200
60.6	1,280	26	.....	1.20	4.78		
60.3	1,460	26	1,392	1.68	7.77		
58.3	1,040	27	1,518	0.64	5.39		
54.6	960	22	820	1.18	6.28		
54.6	1,460	27	1,220	1.22	13.34		
54.3	975	25	980	1.39	3.61		
53.7	940	30	810	1.99	3.76		
58.8	1,270	29	1,215	2.00	6.23		
53.7	900	26	820	1.24	3.83		
53.2	1,010	27	1,255	1.68	3.15		
53.6	930	26	1,050	1.71	2.02		
53.9	930	29	1,550	1.34	1.88		
54.8	1,140	29	1,314	2.12	2.30		
54.7	1,410	26	1,540	1 48	1.62	205	130
55.0	1,180	27	1,175	1.54			
55.1	960	29	1,085	2.01	1.91	195	120
54.8	1,340	27	970	1.36	3.17		
53.6	1,280	29	995	1.87	2.88		
53.3	1,360	27	800	1.38	5.65		
52.5	1,337	25	1,080	1.36	4.08	185	120
52.6	1,425	29	1,185	1.66	3.83		
52.4	1,200	29	925	1.40	4.79		
51.6	840	41	1,000	3.39	4.70		
51.7	1,000	41	1,290	3.23	3.64	193	128
51.6	1,000	39	1,040	2.96	5.55		
51.5	1,040	39	1,060	2.90	4.61		
51.7	1,120	38	1,160	2.80	4.98		

TABLE 6.—NEPHRITIS.—

Case Number Name and Date	Temperature Max.	Temperature Min.	Food Total Calories	Food Carbohydrate, Gm.	Food Fat, Gm.	Food N., Gm.	Urine N., Gm.	Excreta N.,[1] Gm.
Case 2 Lee H.								
12/ 4/15	98.0	97.6	1,153	116	56	6.3	7.2	7.8
1/ 5/16	100.6	98.6	1,146	136	51	4.6	7.8	8.3
1/ 6/16	101.8	98.2	447	32	27	3.2	6.8[2]	7.1
1/ 7/16	102.0	98.6	296	14	20	2.5	16.8[3]	17.1
1/ 8/16	103.4	99.8	477	45	20	4.0	16.3	16.7
1/ 9/16	103.0	99.6	544	49	27	3.8	14.6	15.0
1/10/16	102.6	100.6	664	68	31	4.0	14.1	14.5
1/11/16	102.4	100.6	142	12	8	0.7	11.3	12.0
1/12/16	102.0	98.6	412	46	18	2.3	11.1	11.3
Case 9 William S.								
12/4/15	....	....	1,268	140	55	7.2	9.6	10.3
12/5/15	99.2	97.0	1,180	141	43	8.0	7.6	8.4
12/6/15	103.0	99.8	1,470	144	60	9.4	11.1[4]	12.0
Case 7 John C.								
2/ 8/16	Normal							
2/ 9/16	Normal		1,415	189	57	4.4	8.1	8.5
2/10/16	Normal		2,009	285	76	5.3	6.1	6.6
2/11/16	Normal		1,959	269	78	5.2	5.9	6.4
Case 5 Jack K.								
9/4/16	.....		1,569	204	66	4.7	6.8	7.3

1. Excreta nitrogen calculated as urine nitrogen plus 10 per cent. of food nitrogen.
2. 23 hours.
3. 25 hours.
4. 23 hours 25 minutes.

CASE 6.—Frank C., aged 19, born in Italy. Admitted Feb. 23, 1916; died March 27, 1916; chronic interstitial nephritis; uremia.

History.—No cause of nephritis was found. He says he has always been well and has been a very moderate user of alcohol. For many years he has had nocturia; for two and a half months dimness of vision; for two days, severe frontal headache and scanty urine; for one day, nausea and vomiting. He has had no edema.

Physical Examination.—Patient is well developed and well nourished. He is dyspneic, orthopneic, pale; his eyes have a vacant stare, and he is evidently in pain. Breath urinous. He has no edema. Heart: Left border of dulness in the fifth space 1 cm. outside the nipple line; right border at the sternal margin; no murmurs; second aortic sound markedly accentuated. Arteries not markedly sclerosed. Fundi show marked albuminuric retinitis with hemorrhages. He cannot count fingers at 2 feet.

The urine contained a large amount of albumin, many hyaline and granular casts and a few red blood cells. The Wassermann reaction was very faintly positive.

February 24 he had a spastic convulsion lasting forty-five minutes.

—Clinical Data

Nitrogen Balance, Gm.	Body Weight, Kg.	Urine Volume, C.c.	Calories per Kg.	Fluid Intake, C.c.	NaCl Intake, Gm.	Urine NaCl, Gm.	Blood Pressure, Syst.	Blood Pressure, Diast.
−1.5	55.1	570	21	.....	4.30	....	110	80
−3.7	....	260	..	1,278	2.20	0.85	115	85
−3.4	61.5	240	7	980	0.23	Trace		
−14.6	....	600	..	1,160	0.97	Trace		
−12.7	60.7	940	8	1,140	0.56	Trace		
−12.0	60.2	940+	9	745	0.92	Trace		
−10.5	59.1	900+	11	880	1.56	Trace		
−11.3	59.1	640+	2	885	0.39	Trace		
−9.0	55.9	616	7	720	0.65	Trace		
−3.1	....	1,360	..	.....	4.24			
−0.4	64.1	780	18	.....	7.72	....	155	120
−2.6	64.2	1,278	21	.....	4.40	....	178	90
−4.1	70.0	975	22	955	1.55	5.75	230	125
−1.3	70.1	480	29	850	2.10	1.92		
−0.5	69.3	420	28	975	1.89	2.06	236	130
−8.6	58.5	1,750	26	870	3.23	6.92	197	145

The patient was in the calorimeter February 28. He was irrational and very restless, sitting up in the bed at frequent intervals. His condition had not changed much since admission and he still had headache, but he was passing urine freely, 2,300 to 4,300 c.c. per diem, containing 12 to 17 gm. nitrogen and 2 to 8 gm. sodium chlorid. His breath was not so urinous. The blood pressure was 250 mm. systolic; 130 mm. diastolic.

For a time he improved. March 15 his hemoglobin was 56 per cent.; red blood cells, 3,350,000. March 22 the nonprotein nitrogen of the blood was 46 mg.; creatinin, 1 mg. In the spinal fluid the nonprotein nitrogen was 32 mg.; urea, 17 mg. Blood pressure: 220 mm. systolic; 178 mm. diastolic.

March 21 he began to have headache and nausea once more. March 22 he had a convulsion. After this he became blind, grew more toxic, with marked headaches, and on March 27 died. No necropsy was obtained.

February 28 the urine was collected as follows:

Time of Voiding	Volume, C.c.	Specific Gravity
9:00 a. m.....	410	1.010
2:30 p. m.....	425	1.015
5:20 p. m.....	400	1.010
9:10 p. m.....	300	1.010
4:00 a. m.....	600	1.012
6:30 a. m.....	280	1.010

February 28, McLean index 79. CO_2 combining capacity of the plasma in volume per cent., February 24, 66; February 28, 64.

Case 7.—John C., aged 61, watchman. Admitted Feb. 8, 1916; transferred to City Hospital Feb. 18, 1916, improved; chronic interstitial nephritis.

History.—Thirty-five years prior to test he had urethritis and probably lues. Six years prior he had rheumatic pains in the left shoulder. He has been an excessive pipe smoker but a moderate user of alcohol. In spite of his 61 years he still had the sexual vigor of a young man.

Two years prior to test his joints ached and he was told that his blood pressure was 288 mm. For the five months previous to examination he had been unable to work on account of failing eyesight. He has been dyspneic on climbing two flights of stairs. At times he has severe frontal headaches, dizziness and occasionally loses control of his tongue and becomes aphasic. He has marked frequency of urination, six to eight times in the day, four or more times at night.

Physical Examination.—Well nourished; looks younger than his age. His respirations are deep and regular. He is orthopneic but not cyanotic or edematous. The teeth are in very bad condition. Heart: Apex beat in the sixth space 15 cm. from the median line; second aortic sound much accentuated. There is a large, deep scar on the penis.

Urine: February 8 the phthalein output was 25 per cent. in two hours. February 9 to 12 the daily urine volume was 400 to 1,000 c.c.; nitrogen, 6 to 8 gm.; sodium chlorid 2 to 6 gm. His temperature was normal; pulse 60 to 88; respiration 14 to 22. The blood pressure on two examinations was 285 and 236 mm. systolic; 165 and 130 mm. diastolic. February 8 the McLean index was 136 and the CO_2 combining power of the plasma was 69 volumes per cent.

Case 8.—Mildred C., aged 39, milliner, born in England, single. Admitted Nov. 23, 1915; discharged improved, Jan. 6, 1916. Chronic interstitial nephritis; uremia; hyperthyroidism (?).

History.—Three years prior to admission she had diphtheria. In August, 1915, while on a street car, she began to suffer from headache and vomiting and was brought to Bellevue, where she remained unconscious for four days, and was discharged two weeks later. At this time the urine contained much albumin and many hyaline and granular casts. The Wassermann reaction was strongly positive.

As long as she can remember she has had severe headaches, with nausea and vomiting. These come about every month but are not related to the menses, which are normal. Her appetite is fair, bowels constipated. For one year she has had marked nocturia.

Following her first stay in Bellevue she went back to work. For a week she has had a severe headache. She has had no dyspnea and no edema.

Physical Examination.—November 23: A thin, nervous woman who looks chronically ill. She is slightly dyspneic and orthopneic. There is moderate exophthalmos but no von Graefe's sign, no goiter, no tremor and only slight tachycardia. Heart: Left border of cardiac dulness is 12.5 cm. from the midsternal line; right border, at right sternal margin; the second aortic sound is accentuated; in the aortic region there is a thrill and a systolic murmur. The lungs are normal. The liver edge, spleen and right kidney are palpable. The knee jerks are exaggerated. Ophthalmoscopic examination, negative.

The urine was acid; specific gravity 1.010 to 1.018; glucose absent; albumin present in large amount; a few granular casts were found but no red blood cells. The blood count showed:

Red blood cells	5,080,000
Leukocytes	7,200
Differential, normal	

The patient was put on a somewhat restricted diet and given chloral, 5 grains, and potassium iodid, 5 grains, every day except December 10, when she was in the calorimeter. She improved steadily and was able to go back to work January 6.

The temperature was normal; pulse, 85 to 100; respiration, 20 to 22. The systolic and diastolic blood pressures were as follows:

	Systolic, Mm.	Diastolic, Mm.
November 23	265	190
December 9	260	170
January 5	250	150

Phthalein test, December 1, first hour, 10 per cent.

November 30 the blood analysis was as follows:

Sugar	105.0	mg.
Chlorids	0.54	per cent.
Urea nitrogen	25.0	mg.
Ammonia nitrogen	3.2	mg.
Uric acid	2.6	mg.
Creatinin	2.0	mg.
Corpuscular volume	36.0	per cent.

December 10 the McLean index was 134.

Feb. 13, 1916, the patient was admitted to Bellevue once more. She had a severe headache the day before admission, followed by a general convulsion. The blood pressure was 240 mm. systolic; 128 mm. diastolic. A few days later she left the hospital in fair condition.

477 First Avenue.

CLINICAL CALORIMETRY

TWENTY-THIRD PAPER

THE EFFECT OF ROENTGEN-RAY AND RADIUM THERAPY ON THE METABOLISM OF A PATIENT WITH LYMPHATIC LEUKEMIA*

JAMES B. MURPHY, M.D.
NEW YORK

J. H. MEANS, M.D.†
BOSTON

AND

J. C. AUB, M.D.
NEW YORK

In this paper there will be presented the results of calorimetric observations made in a case of chronic lymphatic leukemia, both before and after vigorous Roentgen-ray therapy, and also after exposure to radium. The basal metabolism in leukemia will be discussed and the effect of irradiation thereon.

The literature contains but few observations of this sort. Those by Grafe,[1] Magnus-Levy,[2] Kraus,[3] and Bohland[4] being the only ones that we have found suitable for comparison with our own case.

By referring to Table 1, in which the experiments of these several authors are collected,[5] it will be seen that in both forms of leukemia there is invariably a marked rise in the basal metabolism expressed in terms of body surface area. This is found in both types about equally, the average increase over the normal in eight cases of lymphatic leukemia being 52 per cent., and in five of the myelogenous type, 44 per cent.[6]

The cause of the increase is uncertain; Grafe believed it to be due to the active metabolism of the large numbers of premature white

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* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division, Bellevue Hospital.

† Henry P. Walcott Fellow in Clinical Medicine, Harvard University.

1. Grafe, E.: Die Steigerung des Stoffwechsels bei chronischer Leukämie und ihre Ursachen, Deutsch. Arch. f. klin. Med., 1911, **102,** 406.

2. Magnus-Levy, A.: Ueber den Stoffwechsel bei acuter und chronischer Leukämie, Virchows Arch. f. path. Anat., 1898, **152,** 107.

3. Kraus, F.: Ueber den Einfluss von Krankheiten, besonders von anämischen Zuständen, auf den respiratorischen Gaswechsel, Ztschr. f. klin. Med., 1893, **22,** 449.

4. Bohland, K.: Ueber den respiratorischen Gaswechsel bei verschiedenen Formen der Anämie, Berl. klin. Wchnschr., 1893, **30,** 417.

5. A more extended form of this table will be found in Paper 15 of this series, The Archives Int. Med., 1916, **17,** 974.

6. In this discussion the patients S. W. of Kraus and H. of Bohland were omitted, there being some uncertainty as to which type of leukemia they belonged.

blood cells. He based this belief on observations made on the metabolism of leukemic blood which he carried out by several methods, chiefly by Bohr's blood gas pump or the Haldane-Barcroft blood gas analysis apparatus. Calculating from such experiments, he found that in individual cases the oxygen demand of the total number of leukocytes in the body might form as much as 10 per cent. of the patient's total oxygen requirement.

The intensity of the rise in basal metabolism, Grafe found, ran parallel with the clinical severity of the disease.

The total nitrogen metabolism has been studied by numerous investigators. Such observations as those of von Noorden,[7] Magnus-Levy,[8] Taylor,[8] Musser and Edsall,[9] Edsall,[10] Goodall,[11] Stejskal and Erben,[12] Döri[13] and of Cavina[14] seem to show fairly definitely that there is, in chronic leukemia, no increase in nitrogenous metabolism at all comparable with that in the respiratory metabolism. There is either a slight retention, a slight loss, or a balance. In acute leukemia, on the other hand, as shown by Magnus-Levy's and Edsall's cases, there is an enormous increase in protein metabolism. Edsall's patient had a negative nitrogen balance of 22.28 gm. a day while on a nitrogen intake of 7.25 gm.!

A marked increase in the uric acid output has been found by a number of observers. One of Magnus-Levy's cases, on a low food intake, excreted 12.2 gm. of uric acid. Wende[15] reports a case of lymphatic leukemia with a uric acid excretion of 5 gm. The case of acute leukemia of Edsall and the two cases of chronic leukemia of Musser and Edsall all showed an increased uric acid output. Lossen and Morawitz[16] also report two cases with high uric acid elimination.

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8. Taylor, A. E.: Contributions from the William Pepper Laboratory of Clinical Medicine, 1900, No. 2, p. 148.

9. Musser, J. H., and Edsall, D. L.: Study of the Metabolism in Leukemia, Under the Influence of the X-Ray, Tr. Assn. Am. Phys., 1905, **20,** 294.

10. Edsall, D. L.: Case of Acute Leukemia, with Some Striking Clinical Features, Tr. Assn. Am. Phys., 1905, **20,** 279.

11. Goodall, H. W.: Nitrogenous Metabolism in a Case of Chronic Myelogenous Leukemia, Boston Med. and Surg. Jour., 1914, **170,** 789.

12. Stejskal, C. v., and Erben, F.: Stoffwechselversuch bei lymphatischer und lienalmyelogener Leukämie, Ztschr. f. klin. Med., 1900, **39,** 151.

13. Döri, B.: Stoffwechseluntersuchungen bei einer mit Benzol behandelten chronischen leukämischen Myelose, Wien klin. Wchnschr., 1913, **26,** 2034.

14. Cavina, G.: Untersuchungen über den Stoffwechsel bei der lymphatischen Leukämie während der Röntgenbestrahlung, Deutsch. Arch. f. klin. Med., 1913, **110,** 585.

15. Wende, G. W.: Case of Lymphatic Leukemia, Am. Jour. Med. Sc., 1901, **122,** 836.

16. Lossen, J., and Morawitz, P.: Chemische und histologische Untersuchungen an bestrahlten Leukämikern, Deutsch. Arch. f. klin. Med., 1905, **83,** 288.

TABLE 1.—Basal Metabolism in Cases of—

Observer	Type	Patient	Calories per Square Meter per Hour (Mech)
Grafe, E.	Lymphatic	T. S. 1a	68.7
		T. S. 1b	52.0
		T. S. 1c	48.7
	Lymphatic	G. K. 2	36.8
	Lymphatic	C. L. 3a	44.5
		C. L. 3b	46.9
	Lymphatic	M. T. 4	65.0
	Lymphatic	M. D. 5	49.8
	Myelogenous	F. H. 6	53.2
	Myelogenous	M. H. 7	49.8
	Myelogenous	H. B. 8	42.3
Magnus-Levy	Lymphatic	J.	45.1
Kraus, F.	Splenomyelogenous	M. B.	48.7
		M. B.	46.4
		M. B.	45.8
	Splenomyelogenous	W. K.	47.8
		W. K.	46.7
		W. K.	49.4
	Lienalis	S. W.	49.7
		S. W.	49.2
Bohland, K.	Lienalis	H.	51.8
		H.	57.8
		H.	56.7
		H.	54.8
	Lymphatic	R.	55.3
		R.	42.1
		R.	42.9
	Lymphatic and lienalis	L.	48.0
		L.	43.7
		L.	42.9
		L.	59.0
		L.	47.3

* For normal averages those given in Paper 13 of this series (Gephart and Du Bois, The Archives Int. Med., 1916, 17, 913) were used

—Leukemia Collected from the Literature

Per Cent. Above or Below Average Normal*	Total Leukocytes	Per Cent. Polymorpho-nuclears	Per Cent. Leukocytes	Total Red Cells	Per Cent. Hemoglobin
+123	820,000	10	89	3,600,000	40
+69	205,000	10	89		
+58	200,000	5	95	2,400,000	30
+19	40,000	28	72	4,800,000	90
+55	130,000	4	96		
+63	165,000	2	98	3,640,000	75
+87	32,000	12	87	3,800,000	70 to 75
+62	170,000	2	98	3,800,000	80
+53	140,000	95	5	4,700,000	60
+54	180,000	95	5	2,600,000	55
+22	230,000	98	2	.....	75
+30					
+58	450,000	..	..	2,800,000	50
+51					
+49					
+38	230,000	..	..	2,400,000	45
+35					
+42					
+54	345,000 to 425,000	..	..	2,990,000 to 2,720,000	50 to 45
+52		..	..		
+60	Ratio of Whites to Reds = 1:5				
+79					
+76					
+70					
+59	Ratio of Whites to Reds = 1:50				
+21					
+24					
+38	Ratio of Whites to Reds = 1:10				
+26					
+24					
+70					
+26					

In Goodall's case there was a high endogenous uric acid elmination, but this showed marked variation which had no relation to the total nitrogen or to the apparent leukocyte destruction. Goodall concluded that the destructive process might be carried beyond the uric acid stage, and that, also, retention of uric acid might occur for the purpose of new leukocyte formation. Other writers, among them Stejskal and Erben,[12] and Rzentkowski,[17] have found no increase in the uric acid output in chronic leukemia. The latter not only failed to find any increase in the endogenous uric acid elimination, but also on feeding meat, Liebig's extract, or uric acid, failed to get an increase in the exogenous elimination. This suggested that the process of uricolysis was increased over the normal.

Folin and Denis[18] have found that the blood uric acid is markedly increased in leukemia.

A retention of phosphates in leukemia has been found by several writers, Moraczewski,[19] Stejskal and Erben,[12] and Musser and Edsall.[9] The latter believe this retention to be due to the rapid building of leukemic tissue, a tissue especially rich in phosphorus.

Stejskal and Erben found a loss of calcium in their case of lymphatic leukemia.

There seems to be, therefore, plenty of evidence to show that a profound change in the general metabolism may occur in leukemia. Since this is so, and since Roentgen and radium therapy have been used very extensively of late in both types of chronic leukemia, it seemed important to determine the effect of such forms of treatment on the leukemic's basal metabolism.

That the Roentgen ray is capable of producing a change in the metabolism in normal individuals is shown by the experiments of Linser and Sick[20] who found an increase in uric acid and purin bases and a decrease in the leukocytes of the blood after irradiation. Baermann and Linser[21] also found a rise in the total nitrogen. Benjamin and von Reuss,[22] in a normal dog after a single very intense

17. Rzentkowski, K.: Untersuchungen über den Purinstoffwechsel in einem Falle von lymphatischer Leukämie, Zentralbl. f. Biochem. u. Biophysik, 1911. **11,** 717.

18. Folin, O., and Denis, W.: On Uric Acid, Urea and Total Nonprotein Nitrogen in Human Blood, Jour. Biol. Chem., 1913, **14,** 29.

19. Moraczewski, W. v.: Stoffwechselversuche bei Leukämie und Pseudoleukämie, Virchows Arch. f. path. Anat., 1898, **151,** 22.

20. Linser, P., and Sick, K.: Ueber das Verhalten der Harnsäure und Purinbasen im Urin und Blut bei Roentgenbestrahlungen, Deutsch. Arch. f. klin. Med., 1906-1907, **89,** 413.

21. Baermann, G., and Linser, P.: Ueber die lokale und allgemeine Wirkung der Röntgenstrahlen, München. med. Wchnschr., 1904, **51,** 996.

22. Benjamin, E., and v. Reuss, A.: Roentgenstrahlen u. Stoffwechsel, München. med. Wchnschr., 1906, **53,** 1862.

exposure, found a slight rise in the total nitrogen, on a fixed intake, lasting several days, and after the second day an increase in phosphorous pentoxid.

A number of writers, among others Ellis,[23] Morris,[24] Heineke,[25] Helber and Linser,[26] Belot[27] and Harvey[28] have described the histologic action of the Roentgen ray on normal tissues. In general, the effect seems to be a destructive action on the entire hematopoietic system. Such organs as the spleen show a diminution in size and degeneration of the parenchyma after irradiation. The action seems to be particularly active in the case of white blood cells, especially those of the lymphocyte series. The white cells, both in the circulation and in the blood forming organs, are attacked. The nucleus is fragmented first, and after this there is a lysis of the entire cell.

We have not found in the literature any observations on the effect of irradiation on the basal metabolism in normal individuals. The effect of the Roentgen ray has been studied very much more extensively in the case of the leukemic than in that of the normal individual. Since Senn,[29] in 1903, first used Roentgen therapy in leukemia, scores of papers on this subject have appeared. A very extensive bibliography up to 1911 will be found in the paper of Keymling.[30]

The effect of irradiation on the basal metabolism was studied in Grafe's case, T. S. (Table 1). The heat production per square meter per hour having been 68 calories before treatment, fell to 52 calories and later to 48 while under treatment. During this time the leukocyte count fell from 820,000 to 200,000.

The changes in the total nitrogen, uric acid and purin base elimination after Roentgen-ray treatment have been observed by numerous writers. Lossen and Morawitz,[16] in one case of myelogenous leukemia, found that the uric acid elimination, having been high during irradia-

23. Ellis, A. G.: The Pathology of the Tissue Changes Induced by the X-Ray, Am. Jour. Med. Sc., 1903, **125,** 85-96.

24. Morris, R. S.: Action of Roentgen Rays on the Blood, Am. Med., 1905, **10,** 946.

25. Heineke, H.: Experimentelle Untersuchungen über die Einwirkung der Röntgenstrahlen auf innere Organe, Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1905, **14,** 21.

26. Helber, E., and Linser, P.: Experimentelle Untersuchungen über die Einwirkung der Roentgenstrahlen auf das Blut, München. med. Wchnschr., 1905, **52,** 689.

27. Belot, J.: On the Influence of the X-Ray on the Hematopoietic Organs, Arch. Röntgen Ray, 1906, **11,** 67 and 108.

28. Harvey, W. G.: On the Pathological Effects of Röntgen Rays on Animal Tissues, Jour. Path. and Bacteriol., 1908, **12,** 549.

29. Senn, N.: Case of Splenomedullary Leukemia Successfully Treated by the Use of the Roentgen Ray, Med. Rec., New York, 1903, **64,** 281.

30. Keymling, E.: Die Röntgen-therapie der Leukämie, Ztschr. f. Röntgen u. Radiumforsch., 1911, **13,** 306, 337, 428, 453.

tion, returned to normal coincidently with the leukocyte count. In another case of the same disease they found that the uric acid remained high even after irradiation had produced an actual leukopenia. Heile[31] found an increase in both uric acid and purin bases in three cases. Königer,[32] in seven cases of chronic myelogenous leukemia, found a marked change in the uric acid elimination following irradiation. This consisted, first, in a marked increase, and later, in a reduction to a normal figure as the blood picture approached an aleukemic condition. Cavina,[14] on the other hand, found no increase either in uric acid or total nitrogen in a case of lymphatic leukemia while the patient was being treated with the Roentgen ray. The nitrogen balance was invariably positive, although the leukocyte count fell from 60,860 to 24,800.

The cases of Musser and Edsall[9] are especially interesting in this connection. In one of their cases in which the Roentgen ray had no beneficial effect clinically, it likewise had little or no effect on the nitrogenous metabolism, whereas in the other case, in which there was a marked reduction in the number of white cells and clinical improvement, there was a definite increase in uric acid and purin base output, a very striking loss of nitrogen and an increased elimination of phosphorus pentoxid.

The histologic action of the Roentgen ray seems to be essentially the same in leukemia as in normal individuals. It has been described in detail in the papers of Warthin[33] and of Aubertin and Beaujard.[34] The immediate action is that most cells of the hematopoietic organs are either destroyed at once or so damaged that they become so later. This action is especially violent on cells of the lymphatic series. In either the lymphatic or the bone marrow series, however, both young and old cells are attacked, with the result that, although the total number of white cells may be reduced to normal and the blood rendered aleukemic, nevertheless the differential count never becomes normal. Pathologic cells persist even when an absolute leukopenia has been produced. As a number of writers point out, therefore, the treatment is purely palliative, but, owing to the great reduction in the size of the spleen and the general clinical improvement, in many cases is, nevertheless, distinctly worth while.

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31. Heile: Ueber intravitale Beeinflussung autolytischer Vorgänge im Körper, Ztschr. f. klin. Med., 1904, **55,** 508.

32. Königer, H.:. Der Einfluss der Roentgenbehandlung auf den Stoffwechsel bei chronischer myeloider Leukämie, Deutsch. Arch. f. klin. Med., 1906, **87,** 31.

33. Warthin, A. S.: The Minute Changes Produced in Leukemic Tissues by Exposure to Roentgen Rays, Am. Jour. Med. Sc., 1914, **147,** 72.

34. Aubertin, C., and Beaujard, E.: Sur le mode d'action de la radiothérapie dans la leucémie myéloïde, Bull. et mém. Soc. méd. d. hôp. de Paris, Series 3, 1913, **36,** 66.

The effect of radium on the metabolism has been studied by Kikkoji[35] who found a significant increase in the basal metabolism in a case of chronic arthritis and in a normal man, but found no effect in a second case of chronic arthritis. The two cases that showed a rise in basal metabolism likewise showed an increase in total nitrogen and uric acid elimination.

Histologically, as shown by the researches of Proescher and Almquest,[36] radium has much the same action on the blood-cells and hematopoietic organs as the Roentgen ray.

Let us now sum up the various facts gathered from the literature. In the first place, there is good evidence that the basal metabolism is always increased in leukemia.

The metabolism of leukemic blood is more active than that of normal blood.

The nitrogenous balance is usually negative in acute and variable in chronic leukemia.

The endogenous uric acid elimination and the uric acid content of the blood are generally increased.

There is often a retention of phosphates.

The Roentgen ray may or may not have a profound effect on the metabolism in leukemia. When it does, this effect consists in an increased elimination of nitrogen; also of uric acid, the latter, however, returning to a normal figure as the leukocyte count approaches normal.

When the leukocyte count falls as a result of irradiation, there is some evidence to show that the basal metabolism falls coincidently.

METHODS USED

During the period that he was under observation the subject of this research, Anthony W., spent part of the time in the metabolism ward of the Sage Institute, a part at the hospital of the Rockefeller Institute, and a part at Saint Luke's Hospital, New York.

While at the Sage Institute the methods used, both those of calorimetry and the general routine, were as already described in the third and fourth papers of this series.[37] The uric acid in blood and urine

35. Kikkoji, T.: Ueber den Einfluss von Radiumemanation auf den Gesamtstoffwechsel in Organismus, Radium in Biologie und Heilkunde, 1911, **1,** 46.

36. Proescher, F., and Almquest, B. R.: Contribution on the Biological and Pathological Action of Soluble Radium Salts, with Special Reference to Its Therapeutic Value in Pernicious Anemia and Leukemia, Radium, 1914, **3,** 65.

37. Gephart, F. C., and Du Bois, E. F.: The Organization of a Small Metabolism Ward, THE ARCHIVES INT. MED., 1915, **15,** 829; The Determination of the Basal Metabolism of Normal Men and the Effect of Food, ibid., p. 835.

was determined by Benedict's[38] method. For the calorimeter experiments the steamer chair was used.

The Roentgen-ray treatments were given at the hospital of the Rockefeller Institute. The treatment used varied from that generally employed in that the whole surface of the body was exposed to a radiation of low penetration.

The radium treatments were given by Dr. Karl M. Vogel at St. Luke's Hospital. Radium was applied over the splenic region on six occasions in the months of July, August and September, 1916.

HISTORY OF CASE

History.—Anthony W., man, aged 59, single, born in Ireland, was admitted to the Sage Metabolism Ward in Bellevue Hospital April 18, 1916 (chronic lymphatic leukemia). He had been in America since 1898.

Family History.—Gout on both sides of the family; otherwise negative.

Past History.—At the age of 7 he had diphtheria and scarlet fever, which were followed by "dropsy." At 10 years he had typhoid fever. Between the ages of 18 and 25 he had rather severe attacks of migraine. When 33 years old he had pains in the left great toe which, he was told, were due to gout. Four years later he had an attack of sciatica which lasted for six months.

Present History.—Symptoms referable to the present trouble had existed for thirteen months before his admission to Bellevue Hospital (March, 1915), when he began to have intermittent attacks of severe pain in the left lower part of the abdomen. The pain was definitely localized above the crest of the ilium and in the groin. It radiated occasionally to the back and left arm. In October, 1915, he began to notice shortness of breath on slight exertion, with a slight orthopnea at night. In December, 1915, he first noticed a firm mass in the left upper quadrant. About the same time he began to have severe cramp-like contractions in the leg muscles as far as the thigh and in the muscles of the hands. They came frequently during the day, lasted two to three minutes, and were relieved by exercise. In the previous thirteen months he had lost about 50 pounds. His appetite and digestion had been good. He had been constipated and had had a moderate nocturia.

Physical Examination.—A well developed, but poorly nourished man, lying comfortably in bed. His skin, sclerae and mucous membranes are pale. The lower teeth show moderate pyorrhea. The thyroid is not enlarged. The heart is enlarged; the borders percuss 15 cm. to the left and 4 cm. to the right of the midsternal line. At the apex and along the sternal margin there is a rough systolic murmur, loudest and roughest in the third left interspace. The lungs are normal.

The spleen can be felt as a definitely outlined, firm mass, dull to percussion, filling the entire left, upper quadrant, and causing a marked bulging in the left flank. Its greatest length is 33.5 cm.; greatest width 18.5 cm. It extends from 2 cm. to the right of the midsternal line deep into the flank, from 11 cm. above the costal margin to 4 cm. below the umbilical line. In the median line, near the costal margin, are left two definite notches. The liver dulness extends from the fifth rib to the costal margin. There are a few pea-sized, soft glands posterior to the left sternomastoid muscle. There

38. Benedict, S. R., and Hitchcock, E. H.: On the Calorimetric Estimation of Uric Acid in Urine, Jour. Biol. Chem., 1915, **20,** 619. Benedict, S. R.: On the Calorimetric Determination of Uric Acid in Blood, ibid., 1915, **20,** 629.

are larger masses in both axillae and a mass the size of an almond in the left groin. Blood pressure, 142 mm. systolic; 105 mm. diastolic.

His appearance at this time is shown by the accompanying photograph (Fig. 1).

BLOOD ANALYSIS

		Mg. Per 100 C.c.
April 19, 1916.	Urea N.	12.3
	Creatinin	1.3
	Uric acid	6.15
	Glucose	102.0
April 24, 1916.	Nonprotein N.	68.2
	Uric acid	3.0
May 20, 1916.	Uric acid	7.18

URINALYSIS

April 18, 1916.	Light yellow, clear, slightly acid to litmus
	Sp. gr. 1.018
	Albumin Slight trace
	Indican Trace
	Glucose Absent
	Few hyaline casts; few leukocytes and red blood cells

Subsequent Course.—April 18. Through the kindness of Dr. Alexander Lambert, to whom we wish to express our thanks, the patient was transferred to the metabolism ward of the Sage Institute. Previously he had been on the general medical service of Bellevue Hospital, Second Division.

April 19. First calorimeter observation.

April 24. Second calorimeter observation.

April 25. Transferred to the hospital of the Rockefeller Institute.

April 26. Roentgen therapy begun.

April 29. Following Roentgen-ray treatments on two successive days (25th and 26th), the patient did not feel well yesterday; headache, weakness, bowels constipated. Condition better today, however.

April 30. Transferred to metabolism ward of Bellevue Hospital.

May 1. Third calorimeter observation. Transferred to hospital of Rockefeller Institute.

May 10. With continued Roentgen-ray dosage the total white count has come down almost progressively. A few days previous to entrance it was 55,000. Two days ago it was 22,000. Patient has been symptom-free save for tenderness over the spleen at times.

May 18. Transferred to the metabolism ward in Bellevue Hospital.

May 19. Fourth calorimeter experiment. Transferred to hospital of the Rockefeller Institute.

May 20. Five days ago patient had severe nosebleed. Size of spleen remains stationary. At times patient has considerable pain in left flank with tenderness over spleen.

Since coming to hospital patient has noticed a small, non-tender mass in right groin, more prominent on straining. Examination shows a loose, right inguinal ring with impulse and visible bulge on cough.

Repeated Roentgen-ray exposure has caused tanning of the whole skin, with some erythema and desquamation over back and thighs.

June 10. Another slight nose-bleed yesterday. Patient is exercising a little each day; feels very weak, however.

Percussion dulness of heart less in both directions by 1 cm., and the murmur is loudest in fifth space, midclavicular line.

June 26. The spleen is growing in size and is much firmer, with a more prominent edge than on entrance. It has extended to the right 2 cm. The

liver edge is palpable 1.5 cm. below the costal margin. There are palpable almond-sized lymph nodes in the neck on either side, in axillae and groins.

There is erythema and desquamation of the skin over the left chest in the axillary line due to the Roentgen ray. There are several very tender areas over the spleen.

July 18. Admitted to St. Luke's Hospital for radium treatment. In applying radium the splenic region was divided into four equal parts and each part was subjected to a two-hour application of radium, making each period eight hours in all.

Fig. 1.—Anthony W., April, 1916, before treatment.

July 25. Radium applied.
August 10. Radium applied.
August 17. Radium applied.
August 26. Radium applied.
August 30. Discharged from hospital.
September 9. Radium applied.
September 23. Radium applied.

Oct. 24, 1916, entered metabolism ward at Bellevue Hospital. Since his first radium treatment the patient has had no pain and very little tenderness over the spleen. The spleen has grown smaller and he has felt much better.

He has had less dyspnea and can walk as far as one mile (slowly) without fatigue.

Physical Examination shows the heart enlarged to the left, with a soft, blowing systolic murmur at the apex, transmitted to the axilla and toward the sternum. The spleen is distinctly smaller than when he was first observed. His appearance at this time is shown in Figure 2.

October 25. Fifth calorimeter experiment.

Blood Analysis: Uric acid, 3.6 mg. per 100 c.c. of blood.

Fig. 2.—Anthony W., Oct. 25, 1916, after Roentgen and radium treatment.

DISCUSSION OF RESULTS

The basal metabolism in a case of chronic lymphatic leukemia showed a rise of 44 per cent. above the average figure for normal men of the patient's age. This finding is similar to those of Grafe, Magnus-Levy, Kraus and Bohland. The high metabolism in leukemia is especially interesting, because (in one case, at least) there was nothing about the general appearance to lead one to suppose that the metabolism was increased. In Graves' disease, as already pointed out

TABLE 2.—Leukemia. Data of—

Subject, Date, Weight. Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Anthony W. 4/19/16	Prelim.	12:00	.....	.....	.....	.....	.....	.....	.....
75.9 Kg. 1.96 Sq. M.	1	1:00	36.0	34.3	0.76	57.6	0.311	113.6	115.4
	2	2:00	34.5	33.5	0.75	58.8	0.311	110.5	112.2
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Anthony W. 4/24/16	Prelim.	12:02	.....	.....	.....	.....	.....	.....	.....
75.4 Kg. 1.96 Sq. M.	1	1:02	33.4	34.3	0.71	48.0	0.402	.....	102.8
	2	2:02	33.4	32.6	0.75	55.3	0.402	.....	113.0
	Aver.	.....	.....	.....	.....	.....	.....	109.5	.....
Anthony W. 5/ 1/16	Prelim.	11:41	.....	.....	.....	.....	.....	.....	.....
78.8 Kg. 1.97 Sq. M.	1	12:31	27.6	26.8	0.75	39.1	0.296	88.4	88.3
	2	1:41	40.1	36.2	9.80	61.5	0.415	121.1	128.5
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Anthony W. 5/19/16	Prelim.	10:39	.....	.....	.....	.....	.....	.....	.....
75.1 Kg. 1.95 Sq. M.	1	11:39	33.2	30.7	0.79	50.0	0.442	101.9	104.1
	2	12:39	34.4	32.0	0.78	56.0	0.442	106.1	110.7
	Aver.	.....	.....	.....	.....	.....	.....	.....	.....
Anthony W. 10/25/16	Prelim.	11:55	.....	.....	.....	.....	.....	.....	.....
77.8 Kg. 1.98 Sq. M.	1	12:56	30.4	26.1	0.85	46.0	0.592	.....	94.5
	2	1:55	31.3	31.0	0.74	59.2	0.592	.....	103.1
	Aver.	.....	.....	.....	.....	.....	.....	94.4	.....

TABLE 3.—Leukemia.—

Name and Date	Food				Food N., Gm.	Urine N., Gm.
	Total Calories	Calories per Kg.	Carbohydrate, Gm.	Fat, Gm.		
Anthony W. 4/19/16	1,899	25	144	110	11.0	10.2
4/20/16	2,534	33	212	138	14.9	10.3
4/21/16	2,459	32	215	132	13.7	11.8
4/22/16	2,611	34	214	144	15.2	10.4
4/23/16	2,524	33	196	142	15.5	10.9
4/24/16	2,276	..	175	128	14.2	12.0
5/ 1/16	2,037	..	160	113	12.9	10.2

* Excreta nitrogen calculated as urine nitrogen plus 10 per cent. of food nitrogen.

—Calorimeter Observations

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
.....	37.5	..	..	....	..	..	..	....	.....	Basal
110.5	37.4	73	60	0.76	..	..	..	....	.....	Restless
108.2	37.4	71	36	0.74	..	..	..	....	.....	Quiet
.....	.....	..	..	0.75	7	79	14	1.48	57.1	
.....	37.5	..	..	....	..	..	..	....	.....	Basal
104.2	37.5	60	32	0.70	..	..	..	....	.....	Quiet; work-adder very sensitive
110.6	37.5	62	33	0.74	..	..	..	....	.....	Quiet; work-adder very sensitive
.....	.....	..	..	0.72	10	86	4	1.45	55.9	
.....	37.3	..	..	....	..	..	..	....	.....	Basal
79.6	37.2	62	31	0.74	..	..	..	....	.....	50 min. period; very quiet
135.1	37.3	59	44	0.80	..	..	..	....	.....	70 min. period; fairly quiet
.....	.....	..	..	....	9	68	23	1.36	53.2	Per period
.....	37.2	65	..	....	..	..	..	....	.....	Basal
98.5	37.1	65	36	0.79	..	..	..	....	.....	Slightly restless
113.3	37.2	65	31	0.78	..	..	..	....	.....	Slightly restless
.....	.....	..	..	....	11	66	23	1.36	53.4	
.....	37.1	..	..	....	..	..	..	....	.....	Basal
93.3	37.1	53	32	....	..	..	..	....	.....	Fairly quiet (61 min. period)
100.7	37.1	55	38	....	..	..	..	....	.....	Restless; coughed (59 min. period)
.....	.....	..	..	0.78	17	62	21	1.21	47.7	

—Clinical Data

Excreta* N., Gm.	Nitrogen Balance, Gm.	Uric Acid, Gm.	Purin N., Gm.	Body Weight, Kg.	Urine Volume, C.c.	Blood Pressure, Syst.-Diast.
11.3	—0.3	.....	.....	75.9	1,140	168-95
11.8	+3.1	0.522	0.014	76.2	1,220	
13.2	+0.5	0.520	0.017	76.1	1,300	
11.9	+3.3	0.489	0.006	75.1	1,300	
12.5	+3.0	0.500	0.005	76.5	1,310	
13.4	+0.8	0.563	0.038	75.4	1,350	140-98
11.5	+1.4	0.569	0.016	76.8	1,666	

in the Fourteenth Paper of this series, there are a number of manifestations—the profuse sweating, the hot, flushed skin, the tachycardia, etc.—which are probably due to the high metabolism. Practically all such signs were lacking in this leukemic. His skin was not hot or flushed; he had no tachycardia; he may possibly have had a tendency to sweat rather more easily than a normal individual. Moreover, there was no nervous element. He was perfectly placid, was rather interested in the experiments, was not in the least worried by being placed in the calorimeter, and was fairly quiet in all the observations. Nevertheless, he had a very high metabolism. The results of the calorimeter experiments are collected in Table 2.

This increased metabolism was apparently not due to increased combustion of body protein, for the patient was in nitrogen equilibrium on a nitrogenous intake of 13 to 15 gm. per day, and, moreover, he was maintaining his weight on an intake of 2,400 calories. The figures for food and urine analysis are given in Table 3.

An inspection of the respiratory quotients shows them to be rather lower than those of normal individuals who have fasted sixteen hours, but no lower than those of many patients with Graves' disease[39] with a similar increase in metabolism. These low quotients are probably due, as in Graves' disease, to the more rapid consumption of the glycogen store because of the high metabolism.

As to what causes the increased metabolism in leukemia we can not venture an opinion. Grafe thought it was the result of the very active metabolism of young white cells. His experiments on the metabolism of blood do show an increased oxygen consumption in leukemic blood, but he could account for only about 10 per cent. of the total oxygen consumption as being due to leukocytes. Just how he could explain a rise of 40 or 60 per cent. in the basal metabolism on that ground, we do not quite understand.

Grafe's supposition that the high metabolism resulted from the leukocytes, led us to plot the heat production and leukocyte counts of our patient and then, from the literature given in Table 1, to see whether there was any relation between the leukocyte count and the level of the metabolism. Among different cases there was no such relation, but in individual cases there was evidence of a certain parallelism. As the leukocyte count fell, the metabolism did likewise, and vice versa. But the fall in leukocytes is always very much greater than that in the metabolism. This statement applies to Grafe's cases T. S. and C. L., and also possibly to a slight extent to our case, as may be seen by consulting Figure 3. Of course, the lack of relationship between metabolism increase and leukocyte count in different cases

39. Du Bois, E. F.: Metabolism in Exophthalmic Goiter, THE ARCHIVES INT. MED., 1916, **17**, 915.

does not in the least disprove Grafe's theory, for it is rather the rate of production of white cells and not their total number that is the determining factor. Further work on the metabolism of leukocytes could be done to advantage.

Let us now consider what effect the Roentgen rays had on the metabolism. Unfortunately, in this connection we have observations on the basal metabolism only. The data on the nitrogen metabolism

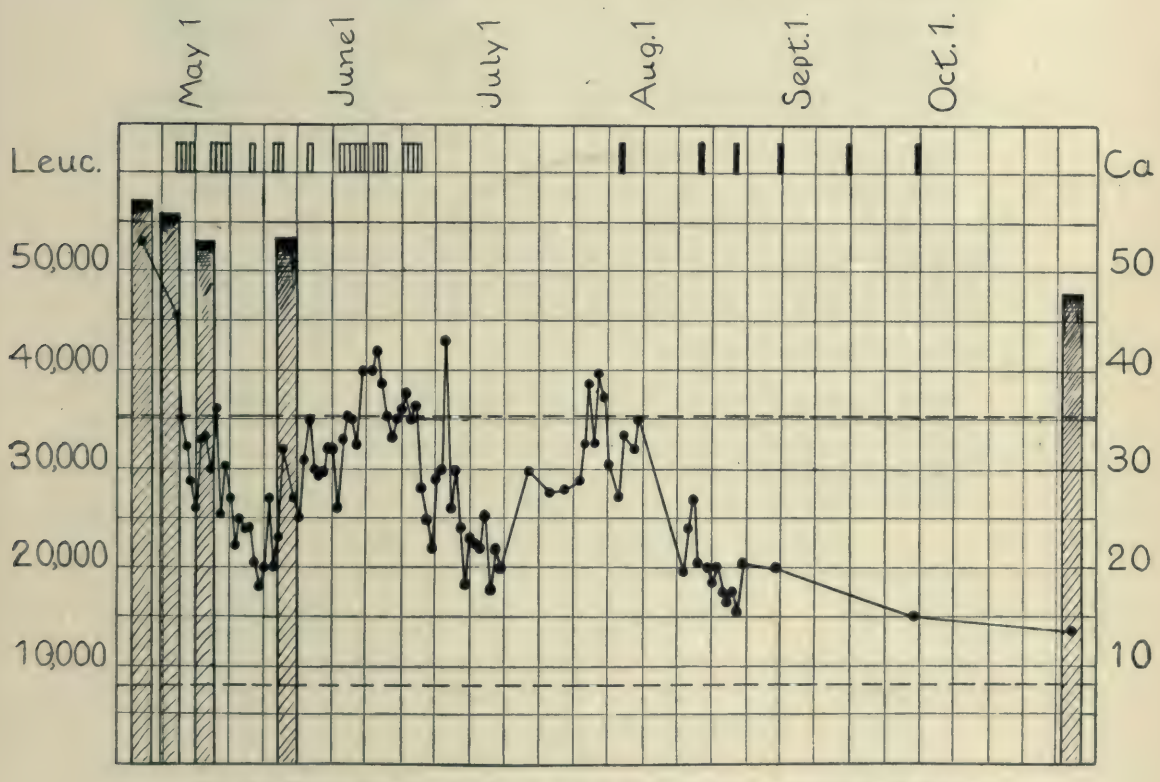

Fig. 3.—Chart showing the basal metabolism, shaded columns, and the leukocyte count, black dots and lines. The hollow rectangles at the top indicate Roentgen treatments, and the black ones radium treatments. The perpendicular rulings indicate periods of one week. The upper broken line represents the average basal metabolism for men from 50 to 60 years of age; the lower, the normal leukocyte count.

were obtained only while the patient was in the Sage metabolism ward, so that all the figures given in Table 3 were obtained before the irradiation was begun.

In Figure 3 the leukocyte count and the basal metabolism are compared. It will be seen that both of these were falling before the irradiation was begun. A slight fall in the basal metabolism occurred five days after the beginning of irradiation but was no greater than

had previously occurred spontaneously, and after twenty-three days, during which ten treatments were given, it had shown no further decrease. The Roentgen ray had no appreciable effect on the basal metabolism in this case. From the appearance of the leukocyte curve it looks as though a drop had been caused in the first few days. Prolonged treatment, moreover, entirely failed to produce an aleukemic blood picture.

The effect of the radium treatment at St. Luke's Hospital is rather more striking. The leukocyte curve shows a much more consistent fall after the radium exposures than after the Roentgen therapy. With this drop in the leukocytes the basal metabolism fell to 47.7 calories per square meter per hour, which is 36 per cent. above the normal average for men of the patient's age.

The results obtained on Anthony W. have recently been confirmed by a patient with myelogenous leukemia studied in the Massachusetts General Hospital in the service of Dr. Edsall. A preliminary report of the findings is given below. The basal metabolism was determined with the small Benedict Universal Respiration Apparatus, using the method of indirect calorimetry.

Dr. J. G., aged 51, height 171 cm. Six months previous to examination it was noticed that the patient's color was not good. For the previous six weeks he had suffered from weakness and lassitude. His blood picture was that of myelogenous leukemia and the spleen was enormously enlarged.

November 9 he felt much better. The size of the spleen was unchanged.

TABLE 4.—Clinical Data in Case of Dr. J. G.

Date	Weight, Kg.	Leukocytes	Basal Metabolism Cals. per Sq. M. per Hr. (Linear Formula)
10/12/16	83.0	296,000	65.3
10/16/16	Radium treatment		
10/17/16	83.0	240,000	60.7
11/ 9/16	81.5	73,000	51.0

DIRECT AND INDIRECT CALORIMETRY

The agreement between the two independent methods of direct and indirect calorimetry in the case of Anthony W. is unusually close. The figure for total calories as measured by the former method is 1,054.0; by the latter method, 1,049.4. This indicates that there is no profound and unsuspected abnormality in the intermediary metabolism.

The water elimination was unusually high, 53 gm. an hour. He lost on an average of 29.5 per cent. of his calories in the vaporization of water under the atmospheric conditions in which normal men lose only 24.1 per cent. in this manner.

SUMMARY AND CONCLUSIONS

A man with chronic lymphatic leukemia was studied five times in the respiration calorimeter. When first observed his metabolism was 44 per cent. above the average normal, falling a little with rest in bed. Intensive treatment with Roentgen rays caused a drop in the leukocyte count but did not appreciably affect the level of his metabolism. The water elimination through skin and respiratory passages was unusually high. Direct and indirect calorimetry gave total results which were almost identical, and no abnormal respiratory quotients were found.

After treatment with radium, a further and very marked fall occurred in the leukocyte count and, at the same time, a slight fall occurred in the basal metabolism.[40]

477 First Avenue.

40. The writers wish to thank Dr. Alexander Lambert for his courtesy in transferring the patient to the metabolism ward; Dr. Montgomery and Dr. Witherbee of the Rockefeller Hospital for the data of Roentgen-ray treatments; and Dr. Karl M. Vogel of St. Luke's Hospital for the data of radium treatments.

CLINICAL CALORIMETRY

TWENTY-FOURTH PAPER

METABOLISM IN THREE UNUSUAL CASES OF DIABETES*

F. C. GEPHART, PH.D., J. C. AUB, M.D.,
E. F. DU BOIS, M.D., AND GRAHAM LUSK, SC.D.
WITH THE TECHNICAL ASSISTANCE OF G. F. SODERSTROM
NEW YORK

The treatment of diabetes by the method of prolonged fasting has been conspicuously successful in recent years. The present paper deals with the measurement of the respiratory exchange and the total heat production of three patients, and supplements Paper 17 of this series by Allen and Du Bois,[1] which contains a review of the literature.

The patients were:

1. A diabetic woman who had been fasted to a state of emaciation, and who had a low tolerance for carbohydrate.

2. A diabetic man who had had the disease in a mild form, who showed a tolerance for 40 gm. of carbohydrate, but who was made completely diabetic (D : N = 3.84) on the second day after the administration of a diet containing considerable quantities of protein and fat. Subsequently, virtual starvation led within sixty hours to the disappearance of the sugar from the urine.

3. A diabetic man who at first manifested resistance to the influence of fasting, whose metabolism indicated complete diabetes, in that he had a D : N ratio of 3.97 when given meat and fat, and also eliminated that quantity of beta-oxybutyric acid theoretically derivable from the fat metabolism of the time. This patient subsequently developed a tolerance for 250 gm. of carbohydrate.

METHODS

The methods and calculations used in these observations were the same as those in the cases previously reported from this laboratory by Allen and Du Bois. The respiratory quotients and total metabolism were determined by the method described in the previous papers on

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*From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division, Bellevue Hospital.

1. Allen, F. M., and Du Bois, E. F.: Metabolism and Treatment in Diabetes, THE ARCHIVES INT. MED., 1916, **17**, 1010.

clinical calorimetry,[2] and, unless otherwise stated, were all basal observations; that is, they were made at least fifteen to eighteen hours after the last ingestion of food. Good alcohol check observations, made just before and after the observations on Cyril K., and at about the same time as the studies of the other two cases reported, assured the accuracy of the findings. The calculations involved in the determination of the protein respiratory quotient, complicated by glucose excretion from protein, were thoroughly discussed in Paper 17 of this series.[3]

Urine: The urinary examinations were made for total nitrogen by the Kjeldahl method; for ammonia, by the Folin method; for urinary sugar, by the Benedict method; for acetone bodies, by Shaffer's method; beta-oxybutyric acid, by Shaffer's method; sodium chlorid, by the Volhardt method.

Blood: Blood sugar was determined by the method of Lewis and Benedict; nonprotein nitrogen, by Bock and Benedict's modification of Folin's method; urea, by the method of Van Slyke and Cullen; blood fat, by Bloor's method. The carbon dioxid combining power of the plasma was determined by the method of Van Slyke; alveolar air determinations were made by the Plesch-Higgins method.

The dextrose to nitrogen ratios are calculated as follows: The carbohydrate value in the food ingested is subtracted from the total glucose found in the urine. The remaining glucose excretion, divided by the total nitrogen excreted during the same period, gives the dextrose to nitrogen value. Its usual maximum value, as first shown by Mandel and Lusk,[4] is 3.65.

ROUTINE

The two male patients were kept in the Sage metabolism ward at Bellevue Hospital under the routine observation described in Paper 3 of this series.[5]

The one female patient was left in the open ward for one day under constant observation of the metabolism nurses. Every attempt was

2. Riche, J. A., and Soderstrom, G. F.: Clinical Calorimetry, Papers 2, 3 and 4, The Respiration Calorimeter of the Russell Sage Institute of Pathology in Bellevue Hospital; Gephart, F. C., and Du Bois, E. F.: The Organization of a Small Metabolism Ward; The Determination of the Basal Metabolism of Normal Men and the Effect of Food, THE ARCHIVES INT. MED., 1915, **15,** 805-867.

3. Allen, F. M., and Du Bois, E. F.: Loc. cit., Note 1, p. 1018.

4. Mandel, A. R., and Lusk, G.: Stoffwechselbeobachtungen an einem Falle von Diabetes mellitus, mit besonderer Berücksichtigung der Prognose, Deutsch. Arch. f. klin. Med., 1904, **81,** 472.

5. Gephart, F. C., and Du Bois, E. F.: Clinical Calorimetry, Paper 3, The Organization of a Small Metabolism Ward, THE ARCHIVES INT. MED., 1915, **15,** 829.

made to have all diets administered as accurately as possible, and composed of simple foodstuffs of known composition. The careful collection of urinary samples, by separate bottles for each voiding, has been described.

REPORT OF CASES

CASE 1.—*History.*—Anna H., aged 31, married, born in United States. Occupation, telephone operator. Weight 32.5 kg.; height 169 cm.

The patient was transferred for one day to Bellevue from the Rockefeller Hospital, where she had been under the care of Dr. Fitz.

Family history and physical history were not remarkable.

She was married three and a half years prior to admission; she had had two miscarriages; health was good until June, 1915. She weighed at that time 145 pounds (66 kg.) with her clothes; then marked polydipsia and polyuria developed, with loss of weight and strength. July 4, 1915, sugar was found in her urine. August 5, a fast of three days made her sugar-free but in September she again had glycosuria.

October 16 she entered the Rockefeller Hospital and remained there five months. She weighed on entrance 49 kg. After fasting six days she became sugar-free, but in order to keep her so she was given a very low diet. For the two months previous to this observation her average total intake was 570 calories a day, made up of whisky (70 to 150 c.c.) and an average of 26 gm. of protein, 17 gm. of fat, and no carbohydrate. This food was taken mostly in the form of eggs. The day previous to the calorimeter determination she received whisky, 30 c.c.; protein, 30.9 gm.; fat, 23.4 gm.; carbohydrate, 2.5 gm., containing in all 458 calories.

The physical examination was negative save for extreme emaciation. Knee jerks were not obtained.

She went into the calorimeter March 31, 1916. During the next few months her tolerance remained low, she lost weight steadily and died July 18, 1916. Permission for necropsy was refused.

Summary.—A case of diabetes of nine months' duration in a young woman. Her sugar tolerance is very low. She can take two to six eggs a day and 100 c.c. of whiskey and remain sugar-free, but if more food is given, sugar appears in the urine. For five months she has been on a very low calory diet at the Rockefeller Hospital (see the foregoing) and her urine has been free from sugar.

I. Her total metabolism is the lowest recorded in the literature, being only 23.2 calories per square meter per hour, which is 37 per cent. below the average basal normal in women. Since her original weight with clothes had been 66 kg., one may be permitted to assume a weight of 62 kg. without clothes. Had her metabolism been normal for this weight, it would have been 63.3 calories per hour instead of 29.4 calories, which were actually measured when her weight had fallen to 32.5 kg. The extreme emaciation which had resulted in a reduction of body weight to nearly half of what it was originally, reduced the metabolism so low that only 40 per cent. of the original heat production was necessary for life. This reduction in metabolism is one of the theoretical benefits of the Allen fasting treatment.

II. The nitrogen excretion in the urine (0.39 gm. per hour) is the quantity commonly found in normal people. The total metabolism, however, is so low that the percentage of calories from protein is quite high, 35 per cent. (15 per cent. being the average normal).

III. The respiratory quotients average 0.82, a normal figure. From this, one may calculate that fat gives 39 per cent. of the calories of metabolism and carbohydrate 26 per cent. This corresponds to the utilization of 44 gm. of carbohydrate daily, and, since none was given in the food, these results are difficult to interpret.

CASE 2 (Table 1).—*History.*—The case of Joseph D. is unusual because of the sudden change from a rather mild diabetes to one of the greatest severity, followed by rapid recovery of sugar tolerance.

Joseph D., aged 33, single, born in Russia. Occupation, carpenter. Admitted to Bellevue Hospital Nov. 9, 1915; discharged Nov. 29, 1915.

The patient was always well until six years prior to admission, when he had a chancre. He took four to five glasses of beer a day and sometimes smoked thirty or forty cigarets a day. His weight three years prior to admission was 89.1 kg.; now it is 56.8 kg.

Three years prior to admission, without known cause, he became very thirsty, hungry and weak. Two years previously sugar was found in the urine. He was given a diet with carbohydrate much reduced in quantity, and also sodium bicarbonate. His urine remained free from sugar for over a year, when he gave up dieting and glycosuria recurred. Then his former symptoms returned; his eyesight had been rapidly failing, so that he had difficulty in reading. For the previous three months he had been at Gouverneur, Bellevue and City Hospitals. He felt well save for weakness and hunger.

Physical Examination.—Emaciated, poorly developed, hollow chested man; face flushed and slightly cyanotic; breath smelled of acetone; tongue deep red and papillae prominent; throat and tonsils deep red and glazed. There was marked clubbing of fingers.

Lungs: Percussion showed dulness at both apices, particularly behind, with narrowing of both apical isthmuses; the breath sounds here were rather sharp and high pitched; voice sounds slightly nasal and tactile fremitus diminished; no râles heard.

Reflexes: Neither knee jerks nor ankle jerks could be obtained.

Extremities: From the knee down there was dulling of sensation for touch, poor differentiation of sharp and dull pressure, and of heat and cold. This was most marked on the inner side of the lower legs.

Wassermann reaction positive.

Blood pressure: systolic, 90 mm.; diastolic, 75 mm.

When transferred to Bellevue Hospital the patient was placed in the metabolism ward. Here his diet was changed from a very liberal allowance to one containing only 1,500 calories, with 40 to 50 gm. of carbohydrate and 15 gm. of nitrogen. With this intake his sugar excretion fell in five days from 72 gm. a day to 22 gm., and the morning urine of the sixth day (November 15) was free from sugar. This led us to believe that the case was comparatively mild, and our opinion was checked by a calorimeter observation. The respiratory quotient was 0.79, a normal value, indicating carbohydrate oxidation.

The patient complained bitterly of low calorie diets, so it was decided to give large quantities of meat and fat. After the calorimeter observation on November 15 he was therefore given a diet containing 3,000 calories, with 25 gm. of protein nitrogen and only 3 gm. of carbohydrate. The diet pleased the patient, but in the following fifteen hours, with 3 gm. carbohydrate in the food, he excreted 25.8 gm. of glucose and 14.9 gm. of nitrogen. The D : N ratio

TABLE 1.—Showing Sudden Change—

Name and Date	Temperature		Food			Food N., Gm.	Urine N., Gm.	Excreta N.,[1] Gm.	Nitrogen Balance, Gm.
	Max.	Min.	Total Calories	Carbohyd., Gm.	Fat, Gm.				
Joseph D. 11/10/16	99.2	98.8	1,521	48	104	14.0	14.6	16.0	—2.0
11/11/16	98.6	97.8	1,495	42	102	14.6	16.8	18.3	—3.7
11/12/16	98.8	97.0	1,576	41	102	15.0	17.8	19.3	—4.3
11/13/16	98.8	97.6	1,724	41	104	14.8	16.8	18.3	—3.5
11/14/16	98.4	98.0	1,580	37	97	13.3	15.9	17.2	—3.9
11/15/16	98.8	98.0	3,067	3	261	24.6	17.9	20.4	+4.4
11/16/16	99.6	98.4	3,135	3	266	25.2	22.8	25.3	—0.1
11/17/16	100.4	98.8	1,849	2	133	12.7	12.3[3]	13.6	—0.8
11/18/16	99.8	99.6	553	?	7	0.5	10.0[4]	10.1	—9.6
11/19/16	98.8	98.0	567	3[2]	17	4.8	9.6[5]	10.1	—5.3
11/20/16	98.8	98.8	674	2	17	3.7	8.5[6]	8.9	—5.2
11/21/16	98.0	97.8	1,091	2	57	4.5	11.2	11.7	—7.1
11/22/16	98.2	97.0	1,318	2	76	6.3	11.9	12.5	—6.2
11/23/16	97.0	97.0	1,527	25	85	7.8	11.5[7]	12.3	—4.5
11/24/16	98.0	97.8	1,615	38	88	9.5	12.1[8]	13.1	—3.6
11/25/16	99.2	97.4	2,120	50	132	12.6	12.3[9]	13.6	—1.0
11/26/16	99.2	98.4	2,059	70	122	12.5	10.6[10]	11.9	+0.7
11/27/16	99.0	98.0	753	22	27	3.9	6.9[11]	7.3	—3.3
11/28/16	98.8	98.0	2,095	56	124	12.3	8.3	10.0	+2.3

1. Excreta nitrogen calculated as urine nitrogen plus 10 per cent. of food nitrogen.
2. Bread crumbs found in bed.
3. 16 hours 55 minutes.
4. 29 hours 35 minutes.
5. 25 hours.
6. 24 hours 30 minutes.

was 1.53. The next day, November 16, the patient felt very well and was allowed to sit in a chair. The diet was continued. The urine of this day showed 90.6 gm. of glucose and a complete D:N ratio, 3.84.

November 17 the diet was reduced to 1,850 calories containing 12.7 gm. of nitrogen and but 2 gm. of carbohydrate. Even with this diet the patient excreted 40.4 gm. of glucose and had a D:N ratio of 3.09. During the day the patient had abdominal pain and marked diarrhea, with mucus and some blood. Toward evening he complained of pain in the left jaw. Six hours after his last meal, which contained 65 gm. of fat and 7 gm. of protein nitrogen, a calorimeter observation was made and the respiratory quotient was found to be 0.714. This value is low, and the calculations show that he was oxidizing almost no carbohydrate. The D:N ratio of 2.53 confirmed the low respiratory quotient.

November 18 the patient was given a very low diet, only 550 calories, mostly in the form of alcohol, with less than 1 gm. of carbohydrate or protein. However, he managed to steal a slice of bread, so that an accurate D:N ratio for the day cannot be given. If one approximately estimates the weight of a slice of bread to be 40 gm., however, the D:N ratio would have been about 2.

A large alveolar abscess was discovered and opened and 2 or 3 c.c. of pus pressed out. The diarrhea stopped and the patient felt well and hungry.

—FROM MILD TO SEVERE DIABETES

Body Weight, Kg.	Urine Volume, C.c.	Calories per Kg.	Blood Pressure, Syst. Diast.	Urine Glucose, Gm.	NH_3N, Gm.	Alcohol, Cals.	Sodium Bicarb., Gm.	D : N Ratio	Acetone plus Diacetic Acid
45.7	1,420	33	.....	71.97	1.295	...	20		
46.3	1,940	33	.....	45.09	0.558	...	20		
46.3	2,040	34	.....	37.45	0.628	80	15		
46.9	3,220	37	.....	32.90	0.584	214	15	....	0.65
47.1	3,420	34	.....	22.20	0.579	187	20	0	0.43
46.0	4,040	..	90-75	25.80	0.707	...	15	1.27	1.77
45.5	3,900	69	95-75	90.57	3.143	...	20	3.84	2.44
44.4	1,392	42	.....	40.38[3]	2.220[3]	281	80	3.09	2.02
44.0	1,060	13	95-75	41.33[4]	1.130[4]	482	25	2.0 (?)	0.58
45.6	3,880	12	.....	2.74[5]	0.585[5]	...	20	1.17[12]	
44.7	3,760	17	95-75	0.00[6]	0.264[6]	441	80		
....	3,880	..	.....	0.00	0.304	441	18		
44.5	3,340	29	.....	0.00	.....	441	10		
44.4	3,400	34	100-80	0.00	.....	441	12		
....	3,620	..	.....	0.00	.....	402			
43.9	3,180	46	.....	0.00	.....	361			
44.7	3,600	42	.....	Trace	.....	321			
....	4,400	..	.....	Sl. trace	.....	321			
....	2,840	..	.....	0.00	.....	401			

7. 25 hours.
8. 23 hours 20 minutes.
9. 23 hours 40 minutes.
10. 24 hours 55 minutes.
11. 23 hours 5 minutes.
12. Eight-hour specimen.

November 19, the respiratory quotient was again nearly normal, 0.775, and by noon the urine was free from sugar.

November 23, the patient was put on a mixed diet with daily increasing carbohydrates.

November 26, with 70 gm. of carbohydrate in the food, there was a faint trace of glucose in the urine.

November 27, low diet day.

November 28, mixed diet containing 50 gm. of carbohydrate. The patient was returned to the hospital from which he had come.

It was difficult to keep this patient on a restricted diet except under constant supervision. This could be managed in the metabolism ward, but not in the open ward.

On further treatment he did not improve, and Jan. 4, 1916, he died in diabetic coma.

Summary.—This case shows very clearly how rapid may be the change in tolerance for carbohydrate in diabetes. The urine of the patient had become free from sugar when given a mixed diet con-

taining 40 gm. of carbohydrate, but the diet high in meat and fat, and alveolar abscess with the diarrhea, were sufficient to make him a complete diabetic; that is, with the theoretical D:N ratio continuing for one day. This is shown in Table 2.

TABLE 2.—Illustrating Rapid Change in Carbohydrate Tolerance

Joseph D., a diabetic whose urine was free from sugar, became completely diabetic (D:N = 3.84) sixteen hours after the ingestion of meat and fat in large quantity, and, on reducing the diet, became free from sugar in about sixty hours.

Date	Day	Diet	Nitrogen in Urine per Hour	D:N	R. Q.	Calories per Sq. M. per Hour	Variation from Normal in Per Cent.
1915 11/15	1	Basal, then high protein...	0.385	....	0.79	37.9	— 5
11/16	2	High protein.....	.....	3.84			
11/17	3	Less protein.....	0.356	2.53	0.714	50.7*	+28*
11/18	4	Fasting and stolen bread					
11/19	5	Fasting and stolen bread..	0.330	0.0	0.78	38.6	— 3

* Restless during both hours while in the calorimeter. Had pain during the last hour and asked to be taken out.

Accompanying this absolute inability to metabolize glucose, there developed at the same time some inability to metabolize fat to its normal end-products. Unfortunately, the only figures we have to report are the values of urinary ammonia and of acetone and diacetic acid excretion. The ammonia values suggest that the formation of acetone bodies was only in moderate quantity.

When the complicating factors were eliminated, the patient rapidly improved and again tolerated a mixed diet of 2,000 calories, containing 50 gm. of carbohydrate.

While the D:N ratio may be altered by the ingestion of carbohydrate food, the respiratory quotient quickly reveals if carbohydrate is being metabolized. The validity of the urinary D:N = 2.53 on November 17 is checked excellently by the calorimeter observations of the same date which showed a very marked drop in the respiratory quotient to 0.714, indicating that very little glucose was being oxidized. Hence, on this day no carbohydrate could have been surreptitiously taken by the patient.

The patient was restless while in the calorimeter on the day of diabetes, so that the increase of 28 per cent. in his metabolism is not to be accepted without qualification. The hourly urinary nitrogen was the same during all three calorimeter periods. It is possible that the

effect of the stimulus due to the high protein metabolism of Day 2 outlasted the presence of the stimulus itself.[6]

CASE 3[7] (Tables 3, 4 and 5).—*History.*—Cyril K., aged 19, single, college student, born in the United States.

The patient was admitted to the Presbyterian Hospital Dec. 7, 1915; transferred to Bellevue Hospital Dec. 14, 1915; retransferred to Presbyterian Hospital Dec. 23, 1915; discharged March 7, 1916.

The family history was negative. The patient's health was always good. Fourteen months prior to admission he passed a life insurance examination. There had been no recent infection. October 19 he weighed 78.2 kg. with his clothes on and was then feeling perfectly well. Early in November he began to lose weight, felt weak, tired, without ambition. November 15 a physician found 4.5 per cent. sugar in the urine. He was given a diet containing much meat, whole wheat bread and buttermilk. He had polydipsia and polyuria. About November 20 he weighed 70.5 kg. with his overcoat on. December 1 he felt drowsy and slept a great deal. December 4 he felt very weak, nauseated and vomited, the drowsiness continuing. His last food was December 6 at 7 p. m.

December 7 he entered Presbyterian Hospital. Hemoglobin, 80 per cent.; white cells, 15,500; Wassermann negative.

Under Dr. Geyelin's care he was fasted until December 11. He seemed to be getting more drowsy; respirations were of the air hunger type; he was nauseated. Each day he received 53 to 114 gm. soda bicarbonate, most of it intravenously.

December 11 he was given food, as fasting did not seem to improve his condition. He received mostly milk and eggs. December 13 his condition improved. He was less drowsy and there was less air hunger.

December 14, transferred to Bellevue Hospital.

Physical Examination.—The patient was 6 feet 2 inches tall; of large frame; very thin, but not yet emaciated, with flushed face, pinched nose, drooping eyelids. He was slightly drowsy, but mentally clear. There was a marked acetone odor to the breath. Respirations were deep, 18 to the minute. The mucous membrane, gums and tongue were bright red and glazed. There were small furuncles on the right pinna and two on the left side of the neck. The remainder of the physical examination was not remarkable.

December 15. Put in the calorimeter this morning after a milk diet.

December 16. The patient read the newspaper; no nausea, said he felt very much better than two days previously. Clinically, he was much improved, although the laboratory findings did not indicate much change. He was placed in the calorimeter after a day of protein food.

December 18. Basal calorimeter observation this morning. Abscess on back of neck incised and 2 c.c. of greenish pus evacuated. Started fasting.

December 19. Abscess dressed; 2 c.c. pus obtained. Blood examination showed: white cells, 10,200; red cells, 5,746,000.

December 20. Basal calorimeter observation.

December 21. Still fasting; patient improving steadily; breathing normal; tongue clean; patient not at all drowsy, but reading all day; abscess still discharging small amount of pus.

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6. Lusk, G.: Animal Calorimetry, Paper 11. An Investigation Into the Causes of the Specific Dynamic Action of the Foodstuffs, Jour. Biol. Chem., 1915, **20,** 569.

7. A preliminary report of this case has been given by Geyelin and Du Bois: A Case of Diabetes of Maximum Severity with Marked Improvement, Jour. Am. Med. Assn., 1916, **66,** 1532. Further details of the clinical and laboratory data will be published shortly by Geyelin.

TABLE 3.—Clinical Data in—

Name and Date	Body Weight, Kg.	Total Calories	Calories per Kg.	Food		Food N, Gm.	Fluid Intake, C.c.	NaCl Intake, Gm.	Sodium Bicarb., Gm.	Chalk, Gm.	Temperature	
				Carbohyd., Gm.	Fat, Gm.						Max.	Min.
Cyril K. 12/14/15	....	936	..	53.0	51.0	9.8	3,430	8.00+	25	15	Normal	
12/15/15	56.7	934	12	24.0	41.0	19.0	5,850	18.00	50	20	Normal	
12/16/15	56.8	458	9	0.4	5.6	16.2	4,525	19.93	55	20	Normal	
12/17/15	58.0	191	3	0.4	2.9	6.3	6,560	27.29	60	30	100.8	98.6
12/18/15	56.5	0	0	Fast	day	....	4,250	10.00	45	20	98.4	97.6
12/19/15	57.2	0	0	Fast	day	1.3	5,550	7.10	55	25	Normal	
12/20/15	56.9	60	1	6.0	0.3	2.6	3,850	8.60	30	20	Normal	
12/21/15	56.6	83	1	6.6	0.3	3.2	4,150	12.12	5	5	Normal	
12/22/15	54.3	108	2	11.4	0.4	3.4	4,050	17.19	..	..	98.2	97.4
12/23/15	....	...	..	....	....	....	.....	.....	..	..	.....	
2/15/16	....	...	..	252.0	6.0	9.5	.....	.....	..	..	.....	
2/16/16	....	...	..	270.0	10.9	7.0	.....	.....	..	..	.....	

* Excreta nitrogen calculated as urine nitrogen plus 10 per cent. of food nitrogen.
† Thirteen hours and forty-five minutes.
‡ Nonprotein nitrogen, 24.7 mg.; blood urea, 9.1 mg.; blood fat, 0.49 per cent.

TABLE 4.—

Subject	Age	Date	Height, Cm.	Weight, Kg.	Surface Area, Linear	Total Calories per Hour	Calories per Sq. M. per Hour
Case 3 (Cyril K.)....	19	12/15/15	187	56.7	1.79	81.9	45.7
		12/16/15	...	56.8	1.79	76.4	42.6
		12/18/15	...	56.5	1.79	73.2	40.8
		12/20/15	...	56.9	1.79	66.3	37.0
		12/22/15	...	54.3	1.75	62.8	35.9
		2/16/16	...	45.8	1.66	43.0	25.9
		3/ 8/16	189	48.3	1.72	50.0	29.1
Case 2 (Joseph D.)	33	11/15/15	170	45.5	1.48	56.1	37.9
		11/17/15	...	44.4	1.47	74.5	50.7
		11/19/15	...	45.6	1.48	57.1	38.6
Case 1 (Anna H.)...	31	3/31/16	169	32.5	1.27	29.5	23.2

* D:N during calorimeter period.

—A CASE OF DIABETES

Blood Pressure Syst. Dias.	Urine Vol., C.c.	Urine* N., Gm.	Nitrogen Balance, Gm.	Urine Glucose, Gm.	D:N Ratio	Urine NaCl, Gm.	NH_3 N., Gm.	Acetone + Diacetic Acid Gm.	Beta-oxy-butyric, Gm.	Alveolar CO_2 Tension, Mm. Hg	Blood CO_2 Vol. %	Blood Glucose, Mg.
.....	4,715	37.7	—28.9	118.5	....	.....	5.41	3.78†	55.2	....	....	.....
118-78	5,290	36.4	—19.8	167.9	3.97	13.21	5.214	5.61	70.9	....	29.2	.....
114-64	5,710	38.3	—23.7	153.4	4.01	16.37	3.537	4.99	75.1	21.0 15.1	28.4	.....
114-78	6,900	36.3	—30.6	140.3	3.87	22.85	3.818	.....	87.4	23.4	51.3	.....
108-60	3,980	20.0	—20.1	55.1	2.76	16.83	2.914	.....	58.5	22.9	52.0	0.150
102-70	4,700	16.7	—15.5	44.3	2.65	15.43	2.290	.....	56.8	30.6	73.9	.....
.....	4,080	14.1	—11.8	35.3	2.44	13.44	1.603	.....	41.2	33.7	75.8	0.177
104-64	6,020	14.4	—11.5	39.7	2.65	19.86	1.524	.....	26.2	....	....	0.170‡
104-70	3,770	18.3	—15.2	26.0	1.12	13.21	1.429	.....	11.0	35.3 31.0	78.2	0.181
.....	.....	....	.....	.....	....	.....	.....	.....	.....	....	72.1	0.206
.....	.....	....	.....	0.0								
.....	.....	....	.....	Trace								

—SUMMARY CHART—DIABETES

Variation from Average Normal, Per Cent.	R. Q.	Nonprotein R. Q.	D : N Ratio*	Per Cent. Calories from			Remarks
				Protein	Fat	Carbohyd.	
+15	0.687	0.699	5.05	21	79	0	After breakfast
+ 7	0.714	0.743	3.65	25	75	0	After breakfast
+ 3	0.707	0.706	2.63	21	79	0	Basal
— 7	0.721	0.718	2.21	15	82	3 (?)	Basal
—10	0.734	0.728	1.53	20	74	6	Basal
—35	0.915	0.970	0.0	31	7	62	Basal
—27	0.860	0.872	0.0	16	37	47	Basal
— 5	0.790	0.787	0.0	17	60	23	Basal
+28	0.714	0.711	2.53	8	90	2 (?)	After dinner
— 3	0.775	0.769	0.0	16	66	18	Basal
—37	0.815	0.822	0.0	35	39	26	Basal

TABLE 5.—Data of Calorimeter—

Subject, Date, Weight. Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 2 (Joseph D.)	Prelim.	11:39 a.m.	....	.....	.....	.....	.....	.....	.....
11/15/15									
45.5 Kg.	1	12:39	18.2	17.3	0.768	28.7	0.385	56.8	53.4
1.48 Sq. M.									
	2	1:39	18.6	16.7	0.812	27.8	0.385	55.4	53.0
Joseph D.	Prelim.	6:04 p.m.	....	.....	.....	.....	.....	.....	.....
11/17/16									
44.4 Kg.	1	7:04	22.6	22.5	0.730	24.1	0.356	73.6	68.1
1.47 Sq. M.									
	2	7:56	19.3	20.1	0.698	23.7	0.356	65.4	59.3
	Aver.	.....	....	.....	.....	.....	.....	.....	.....
Joseph D.	Prelim.	11:43	....	.....	.....	.....	.....	.....	.....
11/19/15									
45.6 Kg.	1	12:43	18.9	17.6	0.780	34.5	0.330	58.2	64.7
1.48 Sq. M.									
	2	1:43	18.0	17.0	0.770	34.1	0.330	56.1	60.2
	Aver.	.....	....	.....	.....	.....	.....	.....	.....
Case 3 (Cyril K.)..	Prelim.	12:31	....	.....	.....	.....	.....	.....	.....
12/15/15									
56.7 Kg.	1	1:31	23.3	23.6	0.718	31.1	1.34	.....	80.1
1.79 Sq. M.									
	2	2:31	25.1	27.3	0.656	36.4	1.34	.....	89.5
	Aver.	.....	....	.....	.....	.....	.....	81.9*	.....
Cyril K.	Prelim.	12:31	....	.....	.....	.....	.....	.....	.....
12/16/15									
5.68 Kg.	1	1:31	24.1	24.5	0.715	32.1	1.44	77.8†	93.6
1.79 Sq. M.									
	2	2:31	23.3	23.7	0.714	31.8	1.44	75.1†	85.9
	Aver.	.....	....	.....	.....	.....	.....	.....	.....
Cyril K.	Prelim.	11:31	....	.....	.....	.....	.....	.....	.....
12/18/15									
56.5 Kg.	1	12:31	22.7	22.3	0.740	31.9	0.927	.....	86.0
1.79 Sq. M.									
	2	1:31	21.5	22.6	0.693	28.0	0.927	.....	81.9
	3	2:31	22.2	23.5	0.688	29.5	0.927	.....	85.1
	Aver.	.....	....	.....	0.707	.....	.....	73.2	.....
Cyril K.	Prelim.	12:12	....	.....	.....	.....	.....	.....	.....
12/20/15									
56.9 Kg.	1	1:12	20.2	20.2	0.728	20.3	0.533	.....	72.5
1.79 Sq. M.									
	2	2:12	20.5	21.6	0.691	22.3	0.533	.....	72.6
	3	3:12	19.9	19.5	0.742	20.6	0.533	.....	67.3
	Aver.	.....	....	.....	0.720	.....	.....	66.4	.....
Cyril K.	Prelim.	11:42	....	.....	.....	.....	.....	.....	.....
12/22/15									
54.3 Kg.	1	12:42	19.7	19.6	0.731	21.4	0.60	63.6	64.2
1.75 Sq. M.									
	2	1:42	19.9	19.5	0.742	21.4	0.60	63.4	67.2
	3	2:42	19.0	19.0	0.729	20.8	0.60	61.5	64.5
	Aver.	.....	....	.....	.....	.....	.....	62.8	.....

* Calculations based on assumed D:N ratio of 3.65.
† Calculations based on assumed nonprotein R. Q. of 0.70.

Direct Calorimetry, Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
....	36.4	....	..	.....	..	..	..	....	.....	Basal; diabetes
51.5	36.4	?	12	0.760	18	67	15	1.25	38.4	Asleep 45 min.
56.6	36.4	68	24	0.814	18	52	30	1.22	37.5	Somewhat restless; awake
....	37.5	[illegible]	..	.....	..	..	..	....	.....	6 hrs. after dinner
77.8	37.8	99	32	0.732	..	..	..	....	.....	Restless
59.5	37.8	103	31	0.697	..	..	..	....	.....	Restless; 52 min. period
....	....	...	..	0.714‡	8	89	3	1.68	50.7	‡Aver. per hour
....	[illegible]	[illegible]	..	.....	..	..	..	....	.....	Basal, second fast day
53.2	36.4	72	20	0.775	15	65	20	....	.....	Reading 30 min.; asleep 10 min.
58.8	36.4	65	13	0.763	16	[illegible]	16	....	.....	Quiet; asleep 30 min.
....	....	....	..	.....	..	..	..	1.25	38.6	
....	37.1	[illegible]	..	.....	..	..	..	....	.....	At 6:30 a.m., ate protein 19, fat 18, carbo. 24
78.5	37.1	[illegible]	15	0.745	..	..	..	....	.....	Quiet; slept 5 min.
82.0	37.0	67	32	0.661	..	..	..	....	.....	Fairly quiet; awake
....	....	....	..	.....	21	79	0	1.44	45.7	Glucose in urine 6.76 gm. per hr.; D:N ratio 5.05
....	37.0	60	..	.....	..	..	..	....	.....	At 6:30 a.m., protein 26, fat 7, carbo. 0; sod. bicarb. at 9 a.m.
[illegible]	[illegible]	65	20	0.743	24	76	0	1.37	43.4	Slightly restless; read 50 min.
75.5	36.8	62	15	0.743	25	75	0	1.32	41.9	Much quieter; awake; did not read
....	....	....	..	.....	..	..	..	....	.....	Glucose in urine 5.24 gm. per hr.; D:N ratio 3.65
....	37.0	62	..	.....	..	..	..	....	.....	Basal; first fast day; sod. bicar. at 9 a.m.
77.2	36.8	63	15	0.750	..	..	..	....	.....	Reading quietly
75.6	36.7	61	5	0.682	..	..	..	....	.....	Reading 15 min.; quiet
74.3	36.5	59	19	0.682	..	..	..	....	.....	Fairly quiet
....	....	....	..	0.706	21	79	0	1.30	40.8	Glucose in urine 2.44 gm. per hr.; D:N ratio 2.63
....	[illegible]	....	..	.....	..	..	..	.. .	.....	Basal; third fast day
68.0	36.2	57	20	.....	..	..	..	....	.....	Quiet; reading
69.4	36.2	56	22	.....	..	..	..	....	.....	Quiet; reading
65.5	36.2	57	14	.....	..	..	..	....	.....	Very quiet
....	....	....	..	0.718	15	82	3	1.17	37.0	Urine glucose 1.18 gm. per hr.; D:N ratio 2.2
....	36.6	....	..	.....	..	..	..	....	.....	Basal; fifth fast day
58.8	36.5	59	14	0.724	20	75	5	....	.....	Reading; quiet
[illegible]	36.5	59	24	0.738	20	71	9	....	.....	Reading 30 min.; slightly restless
68.1	36.6	59	12	0.721	20	76	4	....	.....	Reading 30 min.; quiet
....	....	....	..	.....	..	..	..	1.16	35.9	Glucose in urine 0.92 gm. per hr.; D:N ratio 1.53

TABLE 5.—Data of Calorimeter—

Subject, Date, Weight. Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Fm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Cyril K. ..... 2/16/16 45.8 Kg. 1.66 Sq. M.	Prelim.	11:47	....	.....	.....	.....	.....	.....	.....
	1	12:47	15.8	11.9	0.967	13.7	.....	.....	45.0
	2	1:48	15.3	12.7	0.877	14.1	.....	.....	47.0
	3	2:47	16.8	13.5	0.901	16.7	.....	.....	48.4
	Aver.	.....	....	.....	.....	.....	0.506	43.0	.....
Cyril K. ..... 3/8/16 48.8 Kg. 1.72 Sq. M.	Prelim.	12:58	....	.....	.....	.....	.....	.....	.....
	1	1:58	17.6	14.8	0.866	20.9	0.301	49.9	50.9
	2	2:58	17.5	14.9	0.854	21.3	0.301	50.1	52.6
	Aver.	.....	....	.....	.....	.....	.....	50.0	.....
Case 1 (Anna H.) 3/31/16 32.5 Kg. 1.27 Sq. M.	Prelim.	11:52	....	.....	.....	.....	.....	.....	.....
	1	12:52	10.2	9.2	0.804	17.5	0.390	30.2	31.8
	2	1:52	9.5	8.2	0.840	15.6	0.390	27.2	29.5
	3	2:52	10.4	9.4	0.800	16.1	0.390	30.9	34.2
	Aver.	.....	....	.....	.....	.....	.....	.....	.....

December 22. Basal calorimeter observation. Food given in small amounts; alkali medication discontinued.

December 23. Improving steadily.

December 25. Patient was returned to Presbyterian Hospital. In a week he became permanently sugar-free, and without acetone bodies in his urine.

February 15, 1916, he returned to Bellevue for a calorimeter observation. That day he received 252 gm. of carbohydrate, 60 gm. of protein and 69 gm. of fat without showing sugar in the urine.

February 16, after being in the calorimeter he was given 270 gm. of carbohydrate, 44 gm. of protein and 11 gm. of fat in two and one-half hours. After this large meal he showed only a trace of sugar in his urine.

February 27. A peritonsillar abscess was accompanied by marked lowering of the carbohydrate tolerance.

March 7. Carbohydrate tolerance regained; blood sugar normal, 0.08 per cent. Patient weighed 47.7 kg. He was taking a diet containing 2,500 calories.

March 8. Put in the calorimeter and then sent to his home. Later he developed pulmonary tuberculosis, with high fever.

In February, 1917, the patient was improving somewhat. He died March 17, 1917, having been free from urinary glucose and acetone bodies for 125 days.

The patient was an ideal subject for metabolism study. He was intelligent and anxious to cooperate in all the necessary procedures. He was very quiet when in the calorimeter. The element of increased restlessness frequently observed in disease and suggested by Magnus-Levy[8] as a cause of the increased metabolism sometimes recorded, was therefore absent in this individual.

8. Magnus-Levy, A.: Respirationsversuche an diabetischen Menschen, Ztschr. f. klin. Med., 1905, **56,** 83.

—EXPERIMENTS—DIABETICS—(*Continued*)

Direct Calorimetry, Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
....	34.9	....	..	.....	..	..	..	....	.....	Basal; bed
54.4	35.2	44	7	1.059	..	..	..	....	.....	Very quiet; reading
58.8	35.4	44	9	0.914	..	..	..	....	.....	61 min. period; very quiet
43.2	35.3	44	13	0.945	..	..	..	....	.....	59 min. period; very quiet; reading 50 min.
....	....	....	..	0.970	81	7	02	0.94	25.9	No glucose in urine
....	35.0	....	..	.....	..	..	..	....	.....	Basal
43.1	36.4	....	13	0.879	..	..	..	....	.....	Quiet; reading 15 min.; sleeping 15 min.
43.5	36.2	57	9	0.864	..	..	..	....	.....	Very quiet; reading whole hour
....	....	....	..	0.872	16	37	47	1.03	29.1	No glucose in urine
....	36.1	....	..	.....	..	..	..	....	.....	Basal; in bed
25.7	35.9	60	6	0.805	34	44	22	....	.....	Reading 45 min.
25.5	35.7	57	8	0.864	38	28	34	....	.....	Very quiet; asleep 30 min.
37.8	35.9	59	16	0.797	33	46	21	....	.....	Quiet; reading 10 min.
....	....	....	..	.....	35	39	26	0.91	23.2	

Summary.—This remarkable case may be reported in five successive periods, each sharply distinguished, and in a sixth period observed after an interval of two months. Table 6 represents the average daily figures obtained.

I. First Fasting Period.—The D:N in the urine during three days averaged 2.7 per day. The urinary nitrogen averaged 27.5 gm. daily, which is the highest level of nitrogen excretion ever recorded during fasting. It is threefold the quantity of nitrogen eliminated in ordinary fasting, and, therefore, brings this case of human diabetes in accord with the changes in protein metabolism noted in depancreatized and phlorhizinized dogs. During this period the blood-sugar was at its maximum (0.326 per cent.), beta-oxybutyric acid elimination reached 39.6 gm., and a low carbon dioxid tension in the blood betokened a considerable acidosis. Despite the administration, chiefly by intravenous injection, of between 53 and 114 gm. of sodium bicarbonate daily, the patient became increasingly drowsy, respirations were of the air hunger type, and he suffered from nausea.

II. Mixed Diet Period.—As fasting did not improve the patient's condition, he was given a diet of milk and eggs for four days, and on the third day his condition improved, be became less drowsy and there was less air hunger. After subtracting the carbohydrate ingested from the glucose eliminated in the urine, the D:N may be calculated as 1.9.

Although this indicates an oxidation of carbohydrate, the other metabolism factors of the pathologic complex show little improvement. Thus, the dietary contained 7.2 gm. of nitrogen daily and the urine 34.5 gm., an excess of 27.3 gm. above that contained in the food. The waste of 27.3 gm. of body nitrogen daily compares with a loss of 27.5 gm. daily during the fasting period immediately preceding. During this period of mixed diet the daily quantity of beta-oxybutyric acid eliminated increased to 56.5 gm. and the blood carbon dioxid tension fell to an average level of 22.1 mm. of mercury. It is difficult to find in the evidence presented by the metabolism data any cause for the improvement in the clinical condition.

TABLE 6.—METABOLISM OF CYRIL K.
Weight during Periods I-V, between 57.6 and 54.3 kg.; during Period IV, 45.8 kg.

Period	Date	Length of Period, Days	D:N	R. Q.	Urine		Blood		Calories per Sq. M. Surface	Variation from Normal, Per Cent.
					Nitrogen, Gm.	Beta-oxybutyric Acid, Gm.	Glucose in 100 C.c., Gm.	CO_2 Tension, Mm. Hg		
I. First fasting	1915 Dec. 8–10	3	2.7	.....	27.5	39.6	0.326	28.5		
II. Mixed diet	11–14	4	1.9	.....	34.5	56.5	0.312	22.1		
III. High protein-fat diet	15–17	3	3.9	0.687	37.0	77.8	.....	{19.6} {35.4}	44.1	+11
IV. Second fasting	18–21	4	2.7	0.714	16.3	45.7	0.166	44.4	38.9	— 2
V. Convalescence	22	1	1.1	0.734	18.3	10.9	0.181	52.8	35.9	—10
(Interval, 2 months)										
VI. Recovery	1916 Feb. 10	1	0.0	0.97	12.2	0.0	.....	....	25.4	—36

III. High Protein-Fat Diet Period.—During a period of three days the patient was given a diet of protein and fat, and a D:N ratio of 3.9 was determined. Although no experimental data are available to show why this ratio is higher than 3.65, yet it is possible that the extra sugar may have been derived from a reduction in the quantity of sugar in the body, as would have been indicated by a lowering of the level of blood-sugar. The quantity of "extra sugar," or that eliminated in excess of a D:N ratio of 3.65, may be calculated as being 57 gm. during the three-day period. The patient weighed 57 kg., so that a fall of 0.1 per cent. in the quantity of blood sugar would explain the origin of the "extra sugar." The diet contained an average of 13.7 gm. of nitrogen daily, the urine 37.0 gm., a difference of 23.3 gm., or almost as great a loss of body nitrogen as during the two preceding periods. On the second day of this diet the patient manifested marked clinical improvement, sat up in bed and said he felt much better than two days

before, yet on this day the carbon dioxid tension in the blood fell to its lowest level of 19.6 mm. of mercury, and 75 gm. of beta-oxybutyric acid were eliminated. On the third day, however, the carbon dioxid tension reached 35.4 mm., a level which is more in accord with the actual improvement of the patient. During this period an average of 55 gm. of sodium bicarbonate were given daily.

The beta-oxybutyric acid excretion averaged 77.8 gm. On the two days in which calorimeter investigations were conducted the results may be computed to show how much of the total metabolism of fat reached beta-oxybutyric acid as its terminal stage. When fat is thus oxidized it is theoretically possible for 21.7 per cent. of the quantity of carbon dioxid ordinarily eliminated in the respiration to remain unoxidized in the form of beta-oxybutyric acid. Remembering this, one may make the computation shown in Table 7.

TABLE 7.—BETA-OXYBUTYRIC ACID ELIMINATION

The quantity of beta-oxybutyric acid eliminated per hour was slightly in excess of the quantity derivable from the fat metabolism of the time.

Date	Urine			Calories	CO_2, Gm.	Nonprotein CO_2, Gm.	Theoretical Beta-oxybutyric Acid from Fat, Gm.
	Nitrogen, Gm.	D:N	Beta-oxybutyric Acid, Gm.				
12/15	1.34*	8.97	3.13	81.9	24.2	18.9	3.09
12/16	1.44*	4.01	2.95	76.4	23.7	18.1	2.96

* Eliminated per hour during calorimeter period.

It is apparent from Table 7 that on one of the two successive days the hourly elimination of beta-oxybutyric acid was slightly greater than the quantity derivable from the fat metabolism of the hours spent in the calorimeter. The slight excess may have been due to a slightly greater average of fat metabolism during the twenty-four-hour period than that observed during the calorimeter period, or it may have been due to an origin of beta-oxybutyric acid from those amino-acids which yield it. A considerable origin of beta-oxybutyric acid from the latter source is not indicated.

The picture presented during this period is one in which all the glucose derivable from protein and all the beta-oxybutyric acid formed as an end-product of the oxidation of fat is completely eliminated in the urine. Though Magnus-Levy[9] computed such results for a diabetic and comatose youth, the actual demonstration of this condition is here presented for the first time.

9. Magnus-Levy, A.: Die Acetonkörper, Ergebn. d. inn. Med., 1908, **1**, 385.

The Respiratory Quotient.—An analysis of the diabetic respiratory quotient has already been presented in one of this series of papers.[10] During the period of a high protein-fat diet it is evident that the metabolism was highly abnormal. Only protein and fat were oxidized, and these only partially. It has been shown that when the D : N ratio is 3.65, the protein respiratory quotient becomes 0.632 instead of 0.80 normally, and when beta-oxybutyric acid is produced as the end-product of fat metabolism, the calculated respiratory quotient of fat falls to 0.669 instead of being 0.707, its normal value.

Were this the whole story, one should find agreement between the respiratory quotient as calculated from the end-products of metabolism during the period of severe diabetes and that actually found. Thus, on December 16 when the diabetes was complete, one might calculate the respiratory quotient as follows:

	Respired Gases		
	O_2 Liters	CO_2 Liters	R. Q.
If the D : N were 3.65, then 1.44 gm. N in urine =	4.58	2.91	0.63
If 18.1 gm. nonprotein CO_2 be derived from fat less unoxidized beta-oxybutyric acid,	13.77	9.21	0.67
	18.35	12.12	0.66

The respiratory quotient was actually 0.715, and, as a matter of fact, quotients as low as 0.66 have not been reported in trustworthy experiments on the basal metabolism in diabetes. It is evident that some accessory factors must come into play. It is highly probable that the interaction between acid formation and bicarbonate neutralization plays an important rôle in diabetes. Thus, if beta-oxybutyric acid formed from fat neutralizes sodium bicarbonate, the diabetic respiratory quotient for fat would be 0.715 instead of 0.669. Again, if the acid were neutralized with ammonia instead of with bicarbonate, it would have been at the expense of ammonia which normally would have combined with carbon dioxid in urea formation. The carbon dioxid would tend to be liberated in the respiration and the quotient would be increased.

Under certain conditions of recovery from the diabetic condition, respiratory quotients of 0.80 during fasting have been noted by Joslin,[11] and this has been attributed to the oxidation of beta-oxybutyric acid, which gives a respiratory quotient of 0.889. It should be noted, however, that if sodium beta-oxybutyrate be oxidized to bicarbonate of sodium, the respiratory quotient of the substance would be only 0.667. The unknowable interplay of factors which govern the finer details of

10. Lusk, G.: Clinical Calorimetry, Paper 8. On the Diabetic Respiratory Quotient, THE ARCHIVES INT. MED., 1915, **15,** 939.

11. Joslin, E. P.: Treatment of Diabetes Mellitus, New York, 1916, p. 96.

the respiratory quotient in diabetes prevents its precise interpretation. It is sufficient to bear in mind, however, that the quotient of 0.69, which is frequently found in total diabetes, indicates the oxidation of fat with the neutralization of sodium bicarbonate by the beta-oxybutyric acid formed. The following summary compares the respiratory quotients obtained under different conditions in this laboratory:

	D:N	R. Q.	Nonprotein R. Q.
Diabetic man, Cyril K.....	3.97	0.687	0.699
Diabetic man, Gerald S.....	3.50	0.697	0.700
Phlorhizinized dog	3.54	0.687	0.704

December 15 the nonprotein respiratory quotient of Cyril K. was 0.699, which is sufficiently close to 0.715 to indicate that the oxidation of fat proceeded in such a manner that some carbon dioxid was driven off from combined bicarbonate in the blood. December 16, under essentially the same condition of diabetes in its most intense form, the nonprotein respiratory quotient was 0.743. The alveolar tension of carbon dioxid was taken immediately before and immediately after the respiration experiment, and it fell from 0.21 mm. of mercury to 0.15 mm. This suggests an increased neutralization of acid by the blood with expulsion of carbon dioxid. It is this extra elimination of carbon dioxid which may play some part in this otherwise inexplicably high nonprotein respiratory quotient.

Grafe[12] calculated that if all the nitrogen of protein metabolism were eliminated as ammonia, the quotient would rise from the normal of 0.80 to 0.88. When, in our experiments, a correction of the respiratory quotient of protein was attempted because of the large elimination of ammonia, this has not increased the R. Q. more than 0.01.

The total heat production during this period of complete diabetes presents some interesting aspects. The method of calculating the heat produced from protein metabolism in severe diabetes, as described by Lusk,[13] has here been followed.

When the D:N ratio has fallen below 3.65, the effect on the respiratory quotient and the heat value of protein has been calculated by making deductions for the separate periods, remembering that each gram of glucose derived from protein would normally be associated with

Heat production	3.692 cal.
Oxygen absorption	1.067 gm.
Carbon dioxid elimination.....	1.467 gm.

It should be further remembered that when ammonia is converted into urea by union with carbon dioxid, heat is absorbed in the reaction. When abnormally large amounts of ammonia are eliminated in the urine, this heat

12. Grafe, E.: Zur Kenntniss des Stoffwechsels im protrahierten Hungerzustande, Ztschr. f. physiol. Chem., 1910, **65,** 48.

13. Lusk, G.: Jour. Biol. Chem., 1915, **20,** 600.

would be liberated in the body and not in the urea of the urine. Several calculations of this kind showed that such additional heat did not exceed 1 calory an hour.

The ordinary method for calculating the heat value of fat remains unchanged in spite of the abnormal production of beta-oxybutyric acid. For a liter of oxygen when used to oxidize beta-oxybutyric acid gives a heat value of 4.848 calories, if the figure, 4.69 calories per gram given by Emery and Benedict,[14] is adopted as the heat value of this substance. When fat itself is completely oxidized, the heat value of a liter of oxygen is 4.686, but when 100 gm. are oxidized, leaving a residue of 36 gm. of beta-oxybutyric acid, the heat value of a liter of oxygen is reduced to 4.654, a difference of 0.7 per cent.

In a former paper of this series by Allen and Du Bois[1] the question of the level of total metabolism in diabetes mellitus was discussed at length and need here be considered only in relation to the specific case. It has long been definitely known that an increased protein metabolism increases the heat production. Rubner[15] was the first to advance the idea that the increased heat production in experimental diabetes was due to an increased metabolism. Even though a large amount of the energy present in protein be eliminated in the urine as glucose, still the specific dynamic action of protein is present when it is ingested in diabetes.[16]

The total metabolism of Cyril K. during the period of high protein and fat ingestion was found to be 15 and 7 per cent. above the normal standard of metabolism per square meter of surface given in Paper 13 of this series. The high protein metabolism might sufficiently explain this increase.

The analysis of this factor may be accomplished in the following manner: If one assume that the usual normal excretion of protein nitrogen is 0.5 gm. per hour, one may calculate how much in excess of this the protein metabolism was during the hours of calorimeter investigation. Since Aub and Du Bois[17] find that in man, when 100 calories in protein are metabolized, the total heat production increases by 76.4 calories, it is possible to compute by what increment the extra metabolism of protein would increase the heat production. Such a calculation is presented in Table 8.

The first two observations on Cyril K. were made six hours after taking food. It is questionable whether the small amount ingested

14. Emery, A. G., and Benedict, F. G.: The Heat of Combustion of Compounds of Physiological Importance, Am. Jour. Physiol., 1911, **28,** 301.

15. Rubner, M.: Die Gesetze des Energieverbrauchs bei der Ernährung, Leipzig, 1902, p. 370.

16. Lusk, G.: Loc. cit., note 6, p. 555.

17. Aub, J. C., and Du Bois, E. F.: Clinical Calorimetry, Paper 21, THE ARCHIVES INT. MED., this issue.

would have much effect in stimulating metabolism at the time of observation.

It appears from this calculation that the extra heat production noted in Cyril K. was due to the extraordinarily high protein metabolism, and that with the elimination of that factor the metabolism more nearly approximated that to be expected in a somewhat emaciated individual.

The *prognosis,* as based on the laboratory findings of this case, seemed at this point to be most unfavorable and was so pronounced by Allen and by Lusk, while Joslin, who saw the patient at the same time, stated that he would recover.

IV. Second Fasting Period.—Following the period of high protein diet, a second fasting period was initiated, which extended over four days. The D : N ratio was 2.7, as during the first fasting period. There

TABLE 8.—Specific Dynamic Action of Excessive Protein Destruction (Cyril K.)

Date	Urinary Nitrogen in Excess of Normal Basal per Hour	Extra Calories Due to Specific Dynamic Action (Extra N × 26.5 × 0.764)	Total Calories per Hour	Total Calories Minus Calories of Specific Dynamic Action	Calories (minus Calories of Specific Dynamic Action) per Sq. M. per Hour	Per Cent. Average Normal
1915 12/15	0.83	16.8	81.9	65.1	36.4	— 8
12/16	0.93	18.8	76.4	57.6	32.2	—19
12/18	0.42	8.5	73.2	64.7	36.1	— 9
12/20	....	....	66.3	....	37.0	— 7
12/22	....	....	62.8	....	35.9	—10

were three distinct factors which showed improvement over the fasting period of the week before: (a) a lower protein metabolism; (b) a lower level of blood sugar; (c) a higher carbon dioxid tension of the blood. The elimination of beta-oxybutyric acid, however, did not markedly decrease until the fourth fasting day. The patient showed steady improvement throughout this period, read all day and was free from drowsiness.

V. Convalescent Period.—Following the period of four days of fasting, during which the D : N was 2.7, this ratio suddenly broke to 1.1, the quantity of beta-oxybutyric acid eliminated fell to 11 gm., and the respiratory quotient rose in response to the change in metabolism. Although clinically the condition of the patient had shown constant improvement, yet this day was the first to herald the overthrow of all features of the pathologic metabolism. Within a week he became permanently free from glycosuria and from acetonuria.

It is interesting to note that the excretion of beta-oxybutyric acid decreased before the fall in the D : N ratio, as appears in Table 9.

It may reasonably be questioned whether there could possibly have been an increase in the number of sugar molecules liberated in the metabolism of protein on December 21, such as to have been the cause of the improvement in the oxidation of fat, as evidenced by the fall in the quantity of beta-oxybutyric acid excreted. On the other hand, it may well be that the improvement in the conditions for the oxidation of fat may have reduced the acidosis to such an extent as to have beneficially affected the oxidation of glucose. These latter relations have been set forth in a series of papers by Murlin.[18]

Woodyatt[19] has recently stated that the decrease of acidosis in fasting, emaciated diabetics may, in part, be due to the fact that the metabolism may be solely at the expense of protein. Our observations

TABLE 9.—Showing Fall in Beta-Oxybutyric Acid Before Fall in D : N Ratio

Period	Date	D : N	Beta-oxybutyric Acid
IV	12/19*	2.65	56.84
	12/20*	2.44	41.17
	12/21*	2.65	26.21
V	12/22*	1.12	10.95

* Fasting.

do not corroborate this view, for the highest amount of heat from protein yielded during periods of basal metabolism in severe diabetes has never exceeded 23 per cent. of the total heat production.

During the period of high protein-fat diet and of high acidosis the quantity of *sodium chlorid* was less in the urine than in the diet, whereas the opposite conditions obtained during the following period of fasting which resulted in the clearing up of the acidosis.

VI. Recovery. — After an interval of two months the patient returned to Bellevue Hospital and was again placed in the calorimeter for the determination of his basal metabolism. The day before he had partaken of a diet containing:

Protein	60 gm.
Carbohydrate	252 gm.
Fat	6 gm.

18. Murlin, J. R., and Kramer, B.: Pancreatic Diabetes in the Dog, Jour. Biol. Chem., 1916, **27,** 481.

19. Woodyatt, R. T.: Acidosis in Diabetes, Jour. Am. Med. Assn., 1916, **66,** 1910.

There was no sugar in the urine. The determination of the basal metabolism revealed a respiratory quotient of 0.92 and a nonprotein respiratory quotient of 0.97. These results showed that this man was now deriving his energy, 62 per cent. from carbohydrate, 31 per cent. from protein and 6 per cent. from fat. This astonishing result shows that Cyril K., who two months before had been completely diabetic, was now able to derive two-thirds of his basal requirement for energy from the oxidation of carbohydrate.

Before the onset of diabetes the weight of the patient had been approximately 73.6 kg. His minimal recorded weight as the result of the Allen fasting treatment was 45.8 kg., a loss of 27.8 kg., or 38 per cent. The normal basal metabolism of a man weighing 73.6 kg. and having a height of 188 cm. would have been 79 calories. This contrasts with an actual production of energy amounting to only 43 calories per hour when he was reduced to a weight of 45.8 kg. His heat production was therefore only 55 per cent. of what it would have been had he been of his normal weight.

The results calculated from Case 1 may be compared with those of this patient as in Table 10.

TABLE 10.—Comparison of Results in Case 1 with Those of Cyril K., Case 3

Case	Height, Cm.	Original Weight, Kg.	Lowest Weight, Kg.	Lowest Heat Production in Per Cent. of the Original Normal	Variation in Per Cent. from the Normal per Sq. M. of Surface when Heat Production Was Lowest
1	169	62	32.5	40	—37
3	188	74	45.8	55	—35

After three weeks Cyril K. gained 3.5 kg. in weight, and his metabolism was found to be 27 per cent. below the normal for his weight and height, instead of 35 per cent. below when his emaciation was more extreme.

These experiments on individuals indicate how a community may long support itself on restricted rations.

SUMMARY

Three cases of diabetes studied in the respiration calorimeter are reported.

Case 1.—A diabetic woman through prolonged fasting had been brought to a level of metabolism 37 per cent. below the standard level for her height and weight, a metabolism which was only 40 per cent.

of the original normal value before the initiation of fasting. This is the lowest level of metabolism ever recorded.

Case 2.—A patient with a mild case of diabetes, whose urine was free from sugar, became suddenly and completely diabetic on the administration of a high protein-fat diet, and, on fasting, rapidly regained his former tolerance for sugar.

Case 3.—An acute case of complete diabetes which, in high protein metabolism and in high D: N ratios, resembled experimental diabetes in animals. When given meat and fat, the patient not only excreted all the sugar derivable from protein, but he also excreted all the beta-oxybutyric acid derivable from the fat metabolism of the time. Two months later when the metabolism was 35 per cent. below the normal for his height and weight, two-thirds of the total calories were derived from carbohydrate. The case has afforded an opportunity for the discussion of many of the fundamental facts concerning diabetes mellitus.

477 First Avenue.

CLINICAL CALORIMETRY

TWENTY-FIFTH PAPER

THE WATER ELIMINATION THROUGH SKIN AND RESPIRATORY PASSAGES IN HEALTH AND DISEASE*

G. FABIAN SODERSTROM AND EUGENE F. DU BOIS, M.D.

NEW YORK

1. Introduction.
2. The Sources of Error in Technic.
3. Review of the Literature.
4. Methods Used.
5. Water Elimination of Normal Men Under Standard Conditions.
6. Water Elimination of Patients Under Similar Conditions.
7. Summary and Conclusions.

INTRODUCTION

Few clinicians realize the importance of water in the metabolism, and few investigators appreciate the large errors in its measurement. Apparently, there is nothing easier to measure, and this has led many to publish results without careful controls as to accuracy. As a matter of fact, the technic of determining the water of vaporization is exceedingly difficult and there are few things more laborious than the establishment of the water balance of a patient.

Rubner has pointed out that a starving animal can lose practically all of his glycogen and fat and half of his body protein. If he loses about 10 per cent. of the water of his body he dies. In the clinic few attempts are made to measure the water balance of patients whose tissues are becoming dried on account of insufficient water intake in comparison with an increased output. With edematous patients it is the custom to measure the urine and the fluids of the food with the idea of determining the gain or loss of water to the body. Such measurements are very incomplete. as will be shown by the accompanying example of a true balance sheet (Table 1).

Clinicians allow the nurses to make a large error in neglecting the water content of the so-called *solid* foods. Let us take, for example, the following meal: A small dish of farina, a boiled potato, a portion of tomato and lettuce salad, a small dish of junket and an apple. This is a supper that might well be given a nephritic patient, but it contains about 690 gm. water, something over 23 ounces.

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* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division, Bellevue Hospital.

TABLE 1.—Illustrating Water Balance

	Gm.	
Water Intake:		
Drinking water	300	
Water in coffee, milk, soup	580	
Water in "solid foods"	720	
H_2O from oxidation of 100 gm. protein	41	
H_2O from oxidation of 110 gm. fat	118	
H_2O from oxidation of 244 gm. carbohydrate	135	
		1,894
Water Output:	Gm.	
Water in urine	750	
Water in feces	300	
Water vaporized through skin and respiratory passages	700	
		1,750
Plus balance to body		144
Gain in body weight		100

It is the purpose of the present paper to give some idea as to the amount of water lost from the body in vaporization, and to call attention to this neglected factor in the total output. We can try to estimate the so-called *insensible* perspiration by weighing the patient every day and measuring everything taken and excreted. More accurate determinations can be made in a few cases in respiration chambers. Absolutely accurate determinations cannot be made at present, and it seems advisable to take up this point in detail before reviewing the literature of the subject.

Alcohol Checks.—It has been the policy of the Russell Sage Institute of Pathology to publish each year all the alcohol checks made with the calorimeter (Table 2). This enables other investigators to satisfy themselves as to the accuracy of the apparatus at any given time during the experimental season. Occasionally, there will be an error as great as 2 per cent. in some of the measurements. The average errors for the season of 1915-1916 are as follows:

	Per Cent.
Heat	+0.63
Oxygen	−0.25
Carbon dioxid	−0.42

Respiratory quotient 0.665 instead of the theoretical 0.6666. This shows that the calorimeter is still extraordinarily accurate. The usual error of +2.5 per cent. in measuring the water elimination will be discussed later. It is interesting to study the results in the check of April 3, when about one-quarter of the customary amount of alcohol was burned. The measurement of oxygen and carbon dioxid was surprisingly good, but the method of direct calorimetry gave an error of +2.5 calories in three hours. The large calorimeter was never intended to measure a heat production as low as 19 calories an hour, but even for such small amounts, using the method of indirect calorimetry, it compares favorably with any other respiration chamber as yet constructed.

THE SOURCES OF ERROR IN TECHNIC

It is a very simple matter to measure the water vapor entering and leaving a respiration chamber in which a man or a part of his body is confined. The difference would represent the water vaporized from the body were it not for the fact that water clings to the walls and to the contents of every experimental cabinet. Surprisingly few investigators have taken the trouble to see just how much could be lost or gained in this manner. Stohman[1] called attention to the amount of water that could be absorbed by wood and painted metal. Atwater and Benedict[2] tested the accuracy of the water determination of the Middletown calorimeter, and later the question was discussed in detail by Benedict, Riche and Emmes[3] and by Benedict,[4] who found that large amounts of water vapor could be removed from calorimeter walls and from clothes, bedding and other materials contained within them.

In Papers 2 and 11 of this series it was shown by means of alcohol checks that the Sage calorimeter measured very accurately the oxygen, carbon dioxid and heat, but gave an average error of more than 3 per cent. in the determination of the water produced by the flame. The amount of alcohol usually burned each hour gives off about as much heat and carbon dioxid as a man and consumes about the same amount of oxygen, but produces somewhat less than half the water vaporized by most of the subjects. As a result, the air in the box becomes drier and drier and the water vapor deposited on the tinned walls of the calorimeter, on the copper cooling pipes, on the glass windows and the small wooden parts of the air thermometers, is more or less completely removed as the test progresses. During the first few hours of the experiment there may be a plus error of 0.5 to 1.0 gm. an hour, but later it seldom exceeds half a gram. When the wooden bed, pillow, folded sheet, night-shirt, socks and pajamas are in the calorimeter, astonishing amounts of water can be absorbed or given off, depending on the changes in the relative humidity of the air. In order to demonstrate this, three experiments were made. Nov. 17, 1916, the bed and clothing were placed in the calorimeter, the alcohol lamp was adjusted to burn the usual amount of alcohol per hour, and an arrangement was made by which known amounts of water could be dripped on a piece of muslin about a foot square, tacked on a small wooden frame. The total water vapor formed was estimated by adding the

1. Stohman: Landwirthschaftliche Versuchsstationen, 1876, **19,** 81 and 159.
2. Atwater, W. O., and Benedict, F. G.: A Respiration Calorimeter, Carnegie Institution of Washington, Pub. 42, 1905.
3. Benedict, F. G., Riche, J. A., and Emmes, L. E.: Control Tests of a Respiration Calorimeter, Am. Jour. Physiol., 1910, **26,** 1.
4. Benedict, F. G.: A Comparison of the Direct and Indirect Determination of Oxygen Consumed by Man, Am. Jour. Physiol., 1910, **26,** 15.

TABLE 2.—Alcohol Checks—

Date	Hour	Heat				Oxygen		
		Alcohol Burned, Gm.*	Theory, Cals.	Found, Cals.	Error, per Cent.	Theory, Gm.	Found, Gm.	Error, per Cent.
10/29/15	1	12.70	81.2	81.7	+0.6	23.9	24.8	+3.7
	2	12.34	78.9	79.4	+0.6	23.2	22.9	−1.4
	3	12.77	81.7	80.1	−2.0	24.1	23.6	+2.0
	4	12.10	77.4	78.7	+1.7	22.8	23.3	+2.2
Average	...	.....	79.8	80.0	+0.2	23.5	23.8	+1.3
12/13/15	1	11.17	73.5	68.8	−6.0	21.6	21.6	±0.0
	2	10.44	68.7	69.1	+0.6	20.2	20.2	±0.0
	3	10.38	68.3	69.7	+2.0	20.1	20.4	+1.5
Average	...	.....	70.2	69.2	−1.3	20.6	20.7	+0.5
1/19/16	1	11.96	78.7	79.5	+1.0	23.2	22.9	−1.3
	2	12.42	81.7	80.7	−1.2	24.1	25.3	+5.0
	3	12.37	81.4	80.7	−0.8	24.0	24.2	+0.8
Average	...	.....	80.6	80.3	−0.3	23.8	24.1	+1.2
1/21/16	1	11.59	76.3	78.4	+2.7	22.5	22.6	+0.4
	2	11.44	75.3	76.1	+1.0	22.2	22.4	+0.9
	3	11.31	74.4	77.0	+3.5	21.9	21.5	−1.8
Average	...	.....	75.3	77.2	+2.4	22.2	22.2	±0.0
2/18/16	1	11.92	78.4	77.8	−0.7	23.1	22.5	−2.6
	2	11.89	78.2	77.9	−0.4	23.0	23.0	±0.0
	3	11.26	74.1	75.2	+1.5	21.8	21.2	−2.7
Average	...	.....	76.9	77.0	+0.1	22.6	22.2	−1.8
2/25/16	1	11.82	77.8	77.5	−0.4	22.9	22.5	−1.7
	2	11.47	75.5	76.1	+0.8	22.2	22.3	+0.4
	3	11.73	77.2	78.0	+1.0	22.7	22.5	+0.8
Average	...	.....	76.8	77.2	+0.5	22.6	22.4	−0.9
4/ 3/16	1	2.69	17.7	19.1	+7.9	5.21	4.93	−5.4
	2	2.49	16.4	20.4	+24.4	4.82	5.15	+7.0
	3	3.37	22.2	24.5	+10.5	6.53	6.33	−3.1
Average	...	.....	18.8	21.3	+13.3	5.52	5.48	−0.7
4/14/16	1	12.63	83.1	83.3	+0.2	24.5	24.3	−0.8
	2	12.35	81.3	81.1	−0.2	23.9	23.3	−2.5
	3	12.26	80.7	81.3	+0.5	23.8	23.5	−1.3
Average	...	.....	81.7	81.9	+0.2	24.1	23.7	−1.6
4/17/16	1	14.07	174.2	84.4	+0.3	51.3	24.8	−0.2
	2	12.41		90.3			26.4	
	3	13.28	87.4	87.8	+0.5	25.7	25.4	−1.1
Average	...	.....	87.2	87.5	+0.3	25.7	25.5	−0.8
Total.....	...	.....	2,021.7	2,034.6	+0.63	595.3	593.8	−0.25

water produced by the alcohol flame to the water dripped into the box each hour. The results are shown in Table 3, and it will be seen that 24 to 28 gm. of water were lost per hour. The method of dripping water was rather crude, and much water must have been retained by the wooden frame. Even so, it was evident that the bed and clothing, which had been placed in the box when very dry, absorbed a great deal of water as the humidity rose rapidly. After this experiment was over, still more water was vaporized, the air almost

—SEASON 1915-1916

Carbon Dioxid			Water			R. Q.
Theory, Gm.	Found, Gm.	Error, per Cent.	Theory, Gm.	Found, Gm.	Error, per Cent.	Theory, 0.667
21.9	22.1	+0.9	14.7	15.4	+4.8	0.648
21.3	21.4	+0.4	14.3	14.8	+3.5	0.678
22.0	21.5	−2.2	14.8	14.8	±0.0	0.664
20.9	21.0	+0.5	14.0	14.7	+0.5	0.659
21.5	21.5	±0.0	14.4	14.9	+3.4	0.662
19.8	19.7	−0.5	12.9	12.9	±0.0	0.664
18.5	18.3	−1.0	12.1	12.4	+2.4	0.660
18.4	18.4	±0.0	12.1	12.3	+1.7	0.657
18.9	18.8	−0.5	12.4	12.5	+0.8	0.660
21.2	21.0	−0.9	13.9	14.0	+0.7	0.668
21.6	22.2	+2.7	14.4	14.6	+1.4	0.640
22.0	21.6	−1.8	14.4	14.1	−2.0	0.647
21.6	21.6	±0.0	14.2	14.2	±0.0	0.652
20.6	20.4	−0.9	13.5	13.8	+2.2	0.658
20.3	20.1	−0.9	13.3	13.5	+1.5	0.651
20.1	20.0	−0.5	13.1	13.5	+3.0	0.674
20.3	20.2	−0.5	13.3	13.6	+2.2	0.661
21.2	20.9	−1.4	13.9	13.9	±0.0	0.676
21.1	21.0	+0.4	13.8	14.1	+2.1	0.664
20.0	19.9	−0.5	13.1	13.3	+1.5	0.682
20.8	20.6	−0.9	13.6	13.8	+1.4	0.674
21.0	20.6	−1.9	13.7	14.0	+2.2	0.664
20.4	20.4	±0.0	13.3	13.7	+3.0	0.666
20.9	20.8	−0.5	13.6	13.9	+2.2	0.672
20.8	20.6	−0.9	13.5	13.9	+3.0	0.667
4.78	4.61	−3.6	2.98	3.77	+26.0	0.680
4.42	4.69	+5.6	2.89	3.63	+25.0	0.662
5.98	5.90	±0.0	3.93	4.16	+ 6.0	0.688
5.06	5.07	∓0.0	3.26	3.85	+18.0	0.677
22.4	22.3	−0.4	14.7	15.0	+2.0	0.669
21.9	21.7	−0.9	14.3	14.5	+1.4	0.677
21.8	21.5	−1.3	14.2	14.5	+2.1	0.667
22.0	21.8	−0.9	14.4	14.7	+2.0	0.671
47.0	23.0 24.1	+0.6	30.7	15.4 16.6	+4.2	0.676 0.666
23.6	23.6	±0.0	15.4	15.8	+2.6	0.672
23.5	23.6	+0.4	15.4	15.9	+3.2	0.672
545.1	542.8	−0.42	358.0	367.1	+2.51	Av. 0.665

* In all tests the solution contained 92.92 per cent. by weight of ethyl alcohol.

saturated and allowed to stand this way all night. The next morning the calorimeter was opened and the muslin on its wooden frame placed on a copper plate over the chimney of the alcohol lamp. The lamp was lighted, and during the preliminary period of an hour and the first experimental period of thirty minutes, water was dripped on the muslin, raising the humidity to 60 per cent., at which point there appeared the first dew on the polished pipe of the ingoing water

at a temperature of 15.9 C. The dripping of water was then discontinued, and from this time the alcohol flame was the only source of water except for the bed and clothing and wall of the box. The rate of ventilation was then increased until the relative humidity had fallen to 27 per cent. The large amounts of water removed from the calorimeter can be seen in Table 3. December 4, a complete alcohol check was made, but in addition, 20 c.c. extra water was dripped each hour on a small piece of asbestos in an enamel-ware plate over the lamp chimney. The amount of water recovered was from 1.5 to 2.6 gm. an hour less than the total vaporized. The bed and clothing, which had been exposed to comparatively dry air all night, continued to absorb some moisture for several hours after they were exposed to a greater, but uniform, humidity. In this experiment the average error in the water measurement was 6.7 per cent. It could perhaps be reduced to half of this if great care were taken to maintain an even humidity in the calorimeter room all night. This is difficult, but it is now being attempted.

TABLE 3.—Moisture Tests

Length of Period, Minutes	Total H_2O Formed or Dripped into Calorimeter, Gm.	H_2O Removed, Gm.	Errors, Gain or Loss, Gm.	Relative Humidity at End of Period	Remarks
Nov. 17	....	....	.....	38	Water dripped into box
60	53.0	25.0	—28.0	45	
60	50.0	26.0	—24.0	44	Water dripped into box
Nov. 18	....	....	.....	54	
30	30.0	16.0	—14.0	60	Water dripped into box
30	8.0	19.0	+11.0	57	No extra water
30	9.0	18.0	+ 9.0	54	No extra water
60	16.0	40.0	+24.0	33	No extra water
60	17.0	30.0	+13.0	29	No extra water
60	17.0	27.0	+10.0	27	No extra water
Dec. 4	....	....	.....	36	
60	33.9	32.4	— 1.5	37	20 c.c. extra water dripped into box each hour
60	33.6	30.9	— 2.7	33	
60	33.2	30.6	— 2.6	30	
	100.6	93.9			

The Sage calorimeter is probably much better adapted for the accurate determination of water vaporized than any other respiration chamber except the Middletown calorimeter, which was used for periods of several days. Even so, it is doubtful if it is much more accurate than 10 per cent. under ordinary conditions.

REVIEW OF THE LITERATURE

In reading over the many publications on the subject of water vaporization we must bear in mind the large technical errors found in all types of apparatus. Some investigators took the trouble to weigh the clothing of their subjects before and after the experiment, but could not weigh the experimental chamber and its furniture. Some made the error of drying the cabinet before an experiment, not realizing that water could be lost with a rising humidity. Some have even expressed their results in six significant figures, when it is doubtful if the second figure was accurate.

The older work on vaporization is well reviewed by Rubner,[5] Magnus-Levy[6] and Tigerstedt.[7] In 1866 Pettenkofer and Voit[8] found that the water elimination of a fasting man was 814 to 829 gm. a day. Voit's pupil, Rubner, made a very thorough study of the question, and with his assistants published a series of papers which are of great importance. Their value is increased by the fact that they were produced in the same laboratory with comparable experimental methods. Rubner[9] first studied guinea-pigs and dogs, using a small Pettenkofer-Voit chamber and an air calorimeter. He found that animals gave off much more water in dry than in moist air, a drop in the relative humidity from 69 to 31 per cent. increasing the water elimination from skin and lungs twofold or threefold. Water elimination in guinea-pigs increased as the temperature of the air was raised above 15 C.; in dogs it increased with temperatures above 7 C. When the dogs were given meat, thus increasing the heat production, the water elimination was not affected when the surrounding air was cool, but was markedly increased when the air was warm. Rubner found that for different animals the water elimination was not proportional to surface area, but was nearly proportional to body weight. He concludes, also, that variations in the humidity of the air do not affect the metabolism of protein and fat, and cause no significant change in the total heat production. Increasing moisture in the air diminishes the heat loss through vaporization, but correspondingly increases the heat loss through radiation and conduction.

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5. Rubner, M.: Die Gesetze des Energieverbrauchs bei der Ernährung, Leipzig, 1902; Lehrbuch der Hygiene, Leipzig, 1907.

6. Magnus-Levy, A.: In von Noorden's Handbuch der Pathologie des Stoffwechsels, Berlin, 1906, **1.**

7. Tigerstedt, R.: Wärmeverlust des Körpers, in Nagel's Handbuch der Physiologie des Menschen, Braunschweig, 1909, **1,** 581.

8. Pettenkofer, M., and Voit, C.: Untersuchungen über den Stoffverbrauch des normalen Menschen, Ztschr. f. Biol., 1866, **2,** 478.

9. Rubner, M.: Die Beziehung der atmosphärischen Feuchtigkeit zur Wasserdampfabgabe, Arch. f. Hyg., 1890, **11,** 137; Stoffzerzetzung und Schwankungen der Luftfeuchtigkeit, ibid., p. 243; Thermische Wirkungen der Luftfeuchtigkeit, ibid., p. 255.

TABLE 4.—Water Elimination At 15 C.

	Weight, Gm.	H_2O per Kg. per Day	Percentage of Calories Lost in Vaporization
Man	70,000	12.6	22.9
Dog	30,000	12.2	20.5
Dog	4,000	11.5	9.0
Guinea-pig	550	11.3	6.5

Cramer[10] found that salt was excreted by the skin even when the subjects were at rest in a room at low temperature and concluded that there was a continual secretion of insensible sweat. Nuttall[11] found that when a naked man was placed in a cabinet at a temperature of 29 C., changes in the humidity between 12 and 63 per cent. had little influence on the amount of water removed by the apparatus. Wolpert[12] found that light work scarcely increased the water elimination above the resting values, but that heavy work caused a large increase. He found that the variations in the humidity of air next to the body are limited by the clothing and are not as great as the variations in the outside air. When the air temperature was between 15 and 35 C., the wind from a fan diminished the water loss from the body; above and below these points it increased the vaporization. Laschtschenko[13] demonstrated that the drinking of two liters of water had no effect on the amount eliminated through skin and respiratory passages. Rubner[14] made some interesting determinations of the water eliminated

10. Cramer: Ueber die Beziehung der Kleidung zur Hautthätigkeit, Arch. f. Hyg., 1890, **10,** 231.

11. Nuttall: Ueber den Einfluss von Schwankungen in der relativen Feuchtigkeit der Luft auf die Wasserdampfabgabe der Haut, Arch. f. Hyg., 1895, **23,** 184.

12. Wolpert: Ueber den Einfluss der Lufttemperatur auf die im Zustand anstrengender körperlicher Arbeit ausgeschiedenen Mengen Kohlensäure und Waserdampf beim Menschen, Arch. f. Hyg., 1896, **26,** 32; Ueber die Kohlensäure- und Wasserdampf- Ausscheidung des Menschen bei gewerblicher Arbeit und bei Ruhe, ibid., p. 68; Einfluss der Luftbewegung auf die Wasserdampf- und Kohlensäure-Abgabe des Menschen, ibid., 1898, **33,** 206; Ueber den Einfluss des Windes auf die Atmungsgrosse des Menschen, Arch. f. Hyg., 1902, **43,** 21; Ueber den Einfluss der Luftfeuchtigkeit auf den Arbeitenden, ibid., 1899, **36,** 202. Wolpert and Peters: Die Tageskurve der Wasserdampfabgabe des Menschen, ibid., 1906, **55,** 299.

13. Laschtschenko: Ueber den Einfluss des Wassertrinkens auf Wasserdampf- und CO_2-Abgabe des Menschen, Arch. f. Hyg., 1898, **30,** 145.

14. Rubner, M.: Notiz über die Wasserdampfausscheidung durch die Lunge, Arch. f. Hyg., 1898, **33,** 151. Rubner, M., and Von Lewaschew: Ueber den Einfluss der Feuchtigkeitschwankungen unbewegter Luft auf den Menschen während körperlicher Ruhe, ibid., 1897, **29,** 1.

in the breath during various activities. The subject gave off 17 gm. an hour when quiet, 19 gm. when breathing deeply, 28 gm., reading, and 34 gm. singing. Schattenfroh[15] found that a fat man gave off much more water than a thin man in work experiments, and that with an air temperature of 38 C. and relative humidity of 63 per cent., the heat elimination was not sufficient to prevent a rise of body temperature. Rubner[16] makes some important calculations as to the amount of water a man in the tropics must drink in order to provide enough urine to dissolve the urea and also enough sweat to keep the man cool. It is obvious that with an air temperature of 38 C. or higher, vaporization is the only means of dissipating heat from the body. In order that heat may be dissipated, a man requires 4,400 gm. of water on the ordinary European diet, if producing 2,400 calories per day. On an exclusive meat diet he would require 7,600 gm. of water.

A large amount of data in regard to the water elimination of man can be found in the publications of Atwater, Benedict and their associates.[17] These investigators used a large Atwater-Rosa calorimeter in which a man lived for periods of half a day to two weeks. The experiments were not planned as a study of the water elimination, but they are of great value on account of their length and completeness.

The results are summarized by Benedict and Carpenter[18] who have corrected some miscalculations of the earlier publication. The temperature of the calorimeter was about 20 C., and the humidity in the rest experiments comparatively low. In the work experiments, however, the rate of ventilation was not sufficient to prevent a rise in humidity until it reached a point where there was condensation on the cold-water pipes in the ceiling. These helped to remove the moisture from the air and the water which dripped from them was collected and weighed by the subject of the experiment. The relative importance of the various channels of heat loss are calculated by Benedict and Carpenter and also the changing percentage of calories lost in vaporization with different degrees of muscular activity.

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15. Schattenfroh: Respirationsversuche an einen fetten Versuchsperson, Arch. f. Hyg., 1900, **38,** 93.

16. Rubner, M.: Vergleichende Untersuchung der Hautthätigkeit des Europaers und Negers, nebst Bemerkungen zur Ernährung in hochwarmen Klimaten, Arch. f. Hyg., 1900, **38,** 148.

17. Atwater, W. O., and Benedict, F. G.: Experiments on the Metabolism of Matter and Energy in the Human Body, U. S. Dept. of Agriculture, Bull. 136, 1903, pp. 95 and 134. Benedict, F. G.: The Influence of Inanition on Metabolism, Carnegie Institution of Washington, Pub. 77, 1907. Benedict, F. G., and Carpenter, T. M.: The Metabolism and Energy Transformations of Healthy Man During Rest, ibid., Pub. 126, 1910. Benedict, F. G.: A Study of Prolonged Fasting, ibid., Pub. 203, 1915.

18. See Note 17.

TABLE 5.—Apportionment of Heat Loss

	Rest	Work
Radiation and conduction	75.8	45.5
To warm inspired air	2.0	
Heat of urine and feces	0.7	0.4
Water vaporized from lungs	9.8	43.6
Water vaporized from skin	12.2	
Heat equivalent of external muscular work	....	10.5

TABLE 6.—Percentage of Calories Lost in Vaporization

Condition of Activity	Number of Subjects	Heat Eliminated, Cals.	Percentage of Calories Lost in Vaporization
Rest	5	2,266	23.8
Moderate work	2	3,703	30.9
Severe work	3	4,813	39.6
Very severe work	2	8,225	47.6

Benedict,[19] in his first work on inanition, reviews the literature on the water elimination in fasting. He found that the greatest output took place in the waking hours, and that the amount of drinking water had no effect on the amount eliminated. Benedict calculates the water elimination from the lungs by estimating the volume of the respired air and determining the amount of water required to raise its water content to saturation at body temperature. He found that in most experiments the water elimination from the lungs was somewhat less than from the skin. In the second publication on inanition[19] it is possible to follow the water elimination through a long period of fasting, the subject spending each night in a small bed calorimeter at a temperature of about 21 C. He calculates the water vaporized from the lungs as 9.6 to 10.7 gm. per hour, or from 40 to 65 per cent. of the total.

Day of Fast	Relative Humidity	Water Vaporized Gm.
1– 3	52–63	23–29
17–20	39	15–16
27–30	42–49	18–20

19. See Note 17.

Benedict and Joslin[21] studied a number of diabetics in the same calorimeter and give the following figures for the percentage of calories lost in vaporization:

	Per Cent.
9 Normal controls	22.5
4 Severe diabetes	24.0
3 Light diabetes	22.1

In addition to the series of papers from the laboratories of Rubner and Benedict there have been a large number of scattered publications dealing with the water of vaporization. Only a few can be reviewed in this communication. Janssen,[22] in 1883, studied the water elimination from the arms and legs of normals and nephritics and found that vaporization was increased over edematous parts. Masje[23] investigated the radiation of heat from small areas of skin in different parts of the body. Erismann[24] placed the arm in a box and determined the influence of various factors. Von Willebrand[25] used a cabinet which collected the moisture from the skin only, the head of the subject projecting out of the apparatus. With a relative humidity of 40 to 50 per cent. and a temperature of 12 C., 10.5 gm. water per hour were given off by the skin; at 18 C., 13 to 18 gm.; at 28 C., 26 to 27 gm. There was a sudden outbreak of sweat in one case when the temperature reached 30 C.; in the other man, when it rose to 33.5 C. The carbon dioxid elimination from the skin was constant at 0.2 to 0.4 gm. per hour until the outbreak of sweat, when there was a marked rise in the elimination of this gas. Von Willebrand concludes that before the outbreak of visible sweat the so-called *insensible* perspiration was chiefly vaporization from the outer layers of the skin and not the secretion of the sweat glands. Schwenkenbecker[26] used a similar form of apparatus and confirmed the work of von Willebrand on normals. He studied patients with exophthalmic goiter, tuberculosis, nephritis, diabetes, pneumonia, ichthyosis and several other conditions. He deter-

21. Benedict, F. G., and Joslin, E. P.: Metabolism in Diabetes Mellitus, Carnegie Institution of Washington, Pub. 136, 1910.

22. Janssen: Die Hautperspiration beim gesunden Menschen und bei Nephritikern, Deutsch. Arch. f. klin. Med., 1883, **33,** 334.

23. Masje: Untersuchungen über die Wärmestrahlung des menschlichen Körpers, Arch. f. path. Anat., 1887, **17,** 267.

24. Erismann, E.: Zur Physiologie der Wasserverdunstung von der Haut, Ztschr. f. Biol., 1875, **11,** 1.

25. Von Willebrand, E. A.: Ueber die Kohlensäure- und Wasserausscheidung durch die Haut des Menschen, Skand. Arch. f. Physiol., 1902, **13,** 337.

26. Schwenkenbecker, Dr.: Ueber die Ausscheidung des Wassers durch die Haut von Gesunden und Kranken, Deutsch. Arch. f. klin. Med., 1904, **79,** 29. Schwenkenbecker and Tuteur: Wie reagiert der fiebernde Mensch auf eine willkürliche Steigerung seiner Wärmebildung? Arch. f. exper. Path. u. Pharmakol., 1907, **57,** 285. Schwenkenbecker and Inagaki: Ueber die Schweissekretion im Fieber, ibid., 1905, **53,** 365.

mined the rise in water elimination in typhoid fever after giving certain standard diets and followed the results in various stages of the disease. He concludes that with a rising temperature the vaporization from the skin is at the lower normal limit. With a continued temperature it is somewhat raised, and with a falling temperature it is "active" in proportion to the fall in temperature. In the course of a long-continued fever it becomes gradually smaller. Loewy and Wechselman[27] have made an important contribution in the study of three men born without sweat glands. Although they could not sweat, even when exposed to great heat, they were able at ordinary temperatures to lose as much water through the skin as normal controls. Loewy[28] continued the work with normal adults, children, patients with ichthyosis and two who were paralyzed. He found that different parts of the body gave off different amounts per square meter of surface, and that the same part showed large variations at different times. Anything that lowered the temperature of the skin decreased the water elimination. He believes that the insensible perspiration at ordinary temperatures is due to a physical vaporization through the outer skin and not to a secretion of the sweat glands. He confirmed the older observation of Unna that fat rubbed on the skin diminishes the water loss.

Lang[29] studied the influence of food and of tuberculin fever on the water elimination. He gives a good review of the Russian literature.

Staehelin,[30] using a Jaquet respiration apparatus, determined the heat production and water elimination in the night after various standard meals. The percentage of calories lost in vaporization was between 18 and 21 in basal and food experiments. A well planned experiment on a tuberculous patient with nightsweats was almost spoiled by the restlessness of the subject. Niemann[31] gives figures showing the water of vaporization of babies. This determination must present unusual technical difficulties.

Magnus-Levy[32] calculates the amount of water formed in the oxidation of the various foodstuffs as follows:

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27. Loewy and Wechselman: Zur Physiologie und Pathologie des Wasserwechsels und der Wärmerregulation seitens des Hautorgans, Virchows Arch. f. path. Anat., 1911, **206,** 79.

28. Loewy, A.: Untersuchungen über die physikalische Hautwasserabgabe, Biochem. Ztschr., 1914, **67,** 243.

29. Lang: Beobachtungen über die Wasserausscheidung durch Haut und Lungen unter den Einfluss des Fiebers, Deutsch. Arch. f. klin. Med., 1904, **79,** 343.

30. Staehelin: Versuche über Gaswechsel und Energieverbrauch nach Nahrungsaufnahme, Ztschr. f. klin. Med., 1906, **66,** 201; Der respiratorische Stoffwechsel eines Phthisikers während des Nachtschweisses, ibid., 1906, **66,** 241.

31. Niemann: Der respiratorische Gaswechsel in Säuglingsalter, Ergebn. der inn. Med. u. Kinderh., 1913, **11,** 32.

32. Magnus-Levy, A.: In von Noorden's Handbuch der Pathologie des Stoffwechsels, Berlin, 1906, **1,** 424.

	Gm.	For 100 Calories	
100 gm. fat give	107.1	11.3	
100 gm. starch give	55.5	13.3	Av. 11.3
100 gm. protein give	41.3	9.3	
100 gm. alcohol give	117.4	16.8	

On the ordinary mixed diet of 2,500 calories we should, therefore, obtain about 300 gm. water from the oxidation of the hydrogen in the foods.

The extensive literature on the vaporization of water in fever is not reviewed, but will be discussed in a later communication.

METHODS USED

The Sage calorimeter was built primarily to determine the oxygen consumption, carbon dioxid elimination and total heat production. This latter, as determined by the method of direct calorimetry, is the algebraic sum of the heat of radiation and conduction, the heat stored in or lost from the body as the temperature rises or falls, and the heat rendered latent in the vaporization of water. The air within the calorimeter in all the experiments is between 22 and 24 C., and at this temperature the vaporization of 1 gm. of water requires 0.584 calories. If 1 gm. of water is condensed, the same amount of heat is liberated. For this reason the calorimeter measures accurately the total heat eliminated from the subject, even though some of the water vaporized by the skin be deposited on the walls, pipes or bedding. In such a case, part of the calories which are actually lost from the body by the vaporization of water are transferred to the column of "radiation and conduction." Fortunately, this error is not very large until the humidity reaches a point near 60 per cent., when there is condensation of visible dew on the pipes in the ceiling. The water enters these at a temperature of 13 to 16 C. and leaves them 2 to 4 degrees higher, removing in this manner the heat of radiation and conduction. Their surface area is great and they condense large amounts of moisture from the air when it is saturated at their temperature.

Sometimes the patient is sealed in the calorimeter when the walls and bedding have stood in air at a certain degree of humidity, and then the air is made drier by excessive ventilation. This removes not only the water vaporized from the body, but also a certain amount of moisture from the bedding, etc. More frequently, the humidity rises and moisture is absorbed by the contents of the calorimeter. The subject has been discussed under the heading of "Sources of Error in Technic."

We find ourselves, then, with about 300 experiments on patients and normal controls in which the water vapor removed in the ventilating current of air had been determined in hourly periods. No other

group of observations furnishes so much information as to the water vaporized from skin and respiratory passages in disease. The interpretation of the results must be made with great care on account of the unavoidable technical error.

At the very beginning we must put aside certain experiments and exclude them from the tables used in obtaining averages. The first to be ruled out are those in which the water elimination was so great that there was a condensation of moisture on the cold-water pipes. In this group we find a number of experiments on hyperthyroidism, dyspneic conditions and typhoid fever with falling temperature. These are just the cases in which we should like most to measure the increased percentage of calories lost in vaporization. We must also exclude a few cases with very low water output, because the humidity diminished so rapidly. It seems best to retain only the observations in which the relative humidity did not change more than 10 per cent. and did not approach the point of condensation on the cold pipes. This leaves us 175 satisfactory experiments. Using these, we can compare the normal controls and various groups of patients, because they were studied under certain standard conditions which tend to make the errors constant, thus allowing us to compare the results. These conditions are as follows:

The open calorimeter containing the bed, described in Paper 11, is kept at a temperature of 23 to 24 C. on the night before each experiment, the relative humidity of the air during most of the year being rather low, 15 to 40 per cent. At about half past 9 in the morning the subject is dressed in nightshirt, thick cotton pajamas and two pairs of socks; one pair cotton, one woolen. At about half past 10 he is placed in the calorimeter, the apparatus sealed, and the ventilation adjusted at a rate suitable to the estimated heat production. About an hour later the experiment is started. During this preliminary period the humidity usually rises 10 to 20 per cent., and, after the experiment has begun, continues to increase very slowly.

Before October, 1916, the Crowell blower used on the absorber table could not give a rate of ventilation higher than 70 liters per minute, and this was not sufficient to prevent a slight increase in humidity as the experiment progressed. If the subject had a very high metabolism and water elimination, the humidity would increase to 60 to 70 per cent., at which point there would be a condensation on the pipe which contained the ingoing water at a temperature of 13 to 16 centigrade.

In the summer of 1916 a Lehman Brothers' blower was installed. With this it is possible to obtain any rate of ventilation between 50 and 90 liters a minute. Higher speed would be impracticable with the present system of absorbing bottles. Using this new blower, it is possible to remove 50 to 60 gm. of water an hour and prevent condensation. It is also possible to maintain a low and absolutely uniform

humidity with a normal subject, regulating the ventilation according to the reading of a small hair hygrometer suspended just inside the window of the calorimeter. An experiment performed on E. F. D. B., Dec. 17, 1916, using the newer experimental conditions, in which the humidity was maintained very constant, showed that he gave off 37 gm. of water an hour, losing in this manner 29 per cent. of his calories. With the old blower and lower rate of ventilation and increasing humidity, an average of 31 gm. was removed per hour, and the apparent percentage loss in vaporization was 25 per cent.

An effort has been made to keep the tables expressing the results as small as possible. Only those experiments are used which have already been described in detail, and the first three columns enable one to find the paper of this series in which the data have been published. The relative humidity at the start and finish of each experiment was determined by passing 10 liters of air through a U-tube containing concentrated sulphuric acid. The actual weight of water removed from the calorimeter was determined by weighing the large Williams' bottles half filled with sulphuric acid. Finally, the percentage of calories lost in vaporization was calculated, using the method of direct calorimetry to obtain the total calories. Since the latent heat of vaporization enters into the direct calorimetry, it seemed advisable to use this method of total heat production instead of the method of indirect calorimetry which, after all, gives almost identical results in every group of experiments. Comparisons between various groups are made in the terms of percentage of heat lost in vaporization. This had been the standard method of Atwater and Benedict, and it is the logical method, since the chief function of the vaporization of water is the removal of a certain proportion of the heat produced within the body. We might express the findings in terms of grams of water per kilogram, or square meter of surface area, but this would be of no particular significance in those conditions in which the total metabolism is increased or decreased.

WATER ELIMINATION OF NORMAL MEN UNDER STANDARD CONDITIONS

Thirteen normal men were studied in twenty-nine experiments under the standard conditions (Table 7). They gave off an average of 29 gm. of water an hour, and lost in this manner an average of 24 per cent. of their calories. The percentage figures all come between 21 and 28, and these extremes may be considered as representing roughly the normal limits for the given conditions. It is interesting to note that the only woman studied gave off much more water. This may have been the result of different clothing.

Some of the normal men were given meals containing various

TABLE 7.—Normal Controls

Name	Date	Details Published in Paper	Relative Humidity		H_2O, Gm. per Hour	Per Cent. Calories Lost in Vaporization	Remarks
			Start	End			
E. F. D. B.	3/13/13	4	50	54	27	21	Basal experiments
	5/17/13	4	52	45	32	26	
	3/30/14	4	37	39	31	23	
	5/18/14	4	35	37	28	24	
	5/ 6/15	11	33	35	32	26	
	5/ 7/15	11	44	36	33	26	
	4/12/16	20	43	44	32	23	
	4/26/16	20	41	40	30	27	
John L.	3/26/14	11	36	30	25	24	
	4/ 3/14	11	28	30	24	23	
Charles M.	5/ 4/14	4	36	34	28	23	
Albert G.	12/21/14	11	34	36	32	26	
	12/23/14	11	25	32	26	24	
	12/28/14	11	29	30	26	21	
	1/ 8/15	11	32	37	29	25	
	1/ 9/15	11	38	38	33	28	
Richard S.	4/19/15	11	36	32	26	21	
	4/21/15	11	32	30	25	20	
Morris S.	12/17/14	13	27	33	27	23	
A. F. C.	1/21/15	13	31	33	27	26	
J. H. M.	4/21/16	20	40	41	34	25	
J. C. F.	4/27/16	20	41	34	28	22	
	11/10/16	Unpub.	35	27	25	21	
	11/13/16	Unpub.	38	33	29	24	
J. C. A.	4/29/16	20	38	36	30	23	
S. K.	5/16/16	21	39	32	27	28	
G. F. B.	5/23/16	21	42	37	29	26	
Average					29	24	
Emma W.	5/13/15	13	43	35	30	34	Normal woman
	5/17/15	13	38	34	29	33	

amounts of dextrose or protein, thus increasing the heat production (Table 8). In a few cases the water elimination rose to such an extent that the ventilating current could not prevent a condensation on the pipes. In the majority of cases the table shows that the increase in water was merely proportional to the rise in total heat production. It will be noted that large doses of caffein caused a slight rise in the water of vaporization (Table 9).

TABLE 8.—Normal Men. Heat Production Increased by Giving Dextrose or Protein

Name	Date	Details Published in Paper	Relative Humidity		H_2O, Gm. per Hour	Per Cent. Calories Lost in Vaporization	Remarks
			Start	End			
E. F. D. B.	4/ 1/14	4	37	41	32	23	After 10.5 gm. N.
	5/ 8/14	4	43	41	33	25	After 200 gm. dextrose
	5/15/14	4	36	38	30	23	After 200 gm. dextrose
Charles M.	5/ 6/14	4	45	41	33	26	After 200 gm. dextrose
Albert G.	1/ 4/15	13	29	35	31	21	
	1/ 6/15	13	35	33	33	26	
Morris S.	12/18/14	13	30	34	32	25	After 9.66 gm. N.
S. K.	5/12/16	21	29	35	25	23	After 22 gm. N.
Average					32	23	

TABLE 9.—Normal Men After Caffein

Name	Date	Details Published in Paper	Relative Humidity		H_2O, Gm. per Hour	Per Cent. Calories Lost in Vaporization	Remarks
			Start	End			
E. F. D. B.	4/12/16	20	44	50	37	26	Caffein
	4/25/16	20	40	42	34	25	Caffein
J. H. M.	4/21/16	20	41	53	40	25	Caffein
J. C. F.	4/27/16	20	34	38	38	28	Caffein
J. C. A.	4/29/16	20	36	39	35	28	Caffein
Average					36	26	

TABLE 10.—Boys Aged 12 and 13

Name	Date	Details Published in Paper	Relative Humidity		H_2O, Gm. per Hour	Per Cent. Calories Lost in Vaporization	Remarks
			Start	End			
Fabian R. S.	3/20/15	12	33	33	29	28	Basal
J. D. D. B.	3/26/15	12	33	32	26	26	Basal
Raymond M.	4/ 3/15	12	32	34	26	27	Basal
Reginald F.	4/ 5/15	12	37	36	28	27	Basal
Henry B.	4/ 6/15	12	39	33	33	32	Basal
Harry K.	4/ 7/15	12	32	37	27	27	Basal
Arthur A.	4/ 8/15	12	26	24	22	22	Basal
Leslie B.	4/ 9/15	12	30	28	23	27	Basal
Average					27	27	

With the boys 12 and 13 years old it was possible to maintain a very even humidity. Their water elimination was close to the upper limit of the normal adults (Table 10). The group of very old men gave almost exactly the same figure (Table 11). The rate of ventilalation was better suited to the low heat production of the boys and old men than to the greater caloric output of the men in the prime of life. A proportional ventilation might have brought the figures even closer together. Two of the dwarfs, Raphael de P. and Pat W., showed no thyroid involvement. These, grouped with the two legless men, gave the same average as the men of normal shape and size (Table 12). The other three dwarfs, with symptoms of hypothyroidism, showed a slight diminution of water elimination.

TABLE 11.—Very Old Men

Name	Date	Details Published in Paper	Relative Humidity		H_2O, Gm. per Hour	Per Cent. Calories Lost in Vaporization	Remarks
			Start	End			
Andrew O'C.	5/ 8/16	19	44	40	34	28	Old man
Henry L.	3/13/16	19	39	48	33	26	Old man
Charles H.	5/ 3/16	19	38	34	27	28	Old man
Charles W.	5/ 4/16	19	40	34	26	29	Old man
William C.	8/ 2/16	19	27	32	24	23	Old man
John B.	11/ 4/15	19	24	27	22	26	Old man
Average.....	.....	..	..	..	28	27	

TABLE 12.—Dwarfs and Legless Men

Name	Date	Details Published in Paper	Relative Humidity		H_2O, Gm. per Hour	Per Cent. Calories Lost in Vaporization	Remarks
			Start	End			
Robert L.	12/ 9/14	21	30	29	24	24	Legless man
Harry J.	12/11/14	21	29	27	25	24	Legless man
Harry J.	5/ 5/16	21	35	32	25	28	Legless man
Raphael DeP.	3/15/16	21	30	33	22	25	Achondroplastic dwarf
Patrick W.	3/24/16	21	22	29	17	20	Rachitic dwarf
George F.	1/ 7/16	21	20	20	16	20	Pituitary dwarf; cretin (?)
Erwin E.	8/ 6/16	21	16	17	13	21	Cretin (?)
Benjamin L.	4/10/14	14	21	20	11	21	Cretin
	4/23/14	14	19	18	11	24	Cretin

TABLE 13.—Typhoid Fever Patients

Name	Date	Details Published in Paper	Relative Humidity		H_2O, Gm. per Hour	Per Cent. Calories Lost in Vaporization	Rectal Temp. at Start, C.	Change During Exper., C.	Typhoid Period
			Start	End					
Morris S.	10/29/13	7	49	49	34	24	39.6	—0.1	Contin. temp.
	11/17/13	7	35	28	25	21	38.5	+0.5	1st relapse, ascending temp.
	11/18/13	7	38	43	28	22	39.7	+0.4	1st relapse, ascending temp.
	12/13/13	7	27	31	19	18	37.1	0.0	8th day, normal temp.
	12/16/13	7	27	32	21	20	37.3	0.0	11th day, normal temp.
	12/20/13	7	33	40	26	16	39.3	+0.5	2d relapse, early steep curve
	12/23/13	7	36	37	26	19	38.0	+0.6	2d relapse, early steep curve
	1/ 2/14	7	26	31	21	26	37.0	+0.1	8th day, normal temp.
	1/27/14	7	31	33	22	19	37.1	—0.1	33d day, normal temp.
Charles F.	11/15/13	7	37	47	31	23	40.0	+0.1	Contin. temp.
	11/29/13	7	43	40	28	24	36.7	+0.5	Early steep curve
	12/26/13	7	38	37	26	20	36.8	0.0	25th day, normal temp.
	12/31/13	7	30	37	25	22	37.1	—0.1	30th day, normal temp.
Howard F.	11/ 7/13	7	31	34	24	23	39.7	—0.2	Ascend. temp.
	11/13/13	7	33	35	23	22	39.8	0.0	Contin. temp.
	11/20/13	7	42	37	27	28	39.3	—0.4	Contin. temp.
	12/ 2/13	7	28	27	18	22	36.8	+0.1	6th day, normal temp.
	12/ 6/13	7	26	27	18	21	37.0	0.0	10th day, normal temp.
	12/18/13	7	26	35	21	21	37.1	+0.1	22d day, normal temp.
	12/30/13	7	31	35	23	23	37.3	—0.1	34th day, normal temp.
Thomas B.	10/15/13	7	34	42	26	20	36.8	+1.0	Late steep curve
	10/21/13	7	37	42	25	25	36.7	—0.1	1st day, normal temp.
Anton K.	10/16/13	7	52	49	32	27	37.0	+0.2	Late steep curve
Edward B.	10/23/14	7	41	38	30	23	38.1	+0.8	1st relapse, early steep curve
	10/27/14	7	36	35	30	26	37.4	+0.5	1st relapse, late steep curve
	11/ 4/14	7	40	37	32	27	37.2	+0.2	4th day, normal temp.
	11/ 6/14	7	38	35	25	23	38.8	+0.7	2d relapse, ascend. temp.
John K.	12/15/14	7	36	42	37	24	39.0	+0.2	Contin. temp.

WATER ELIMINATION OF PATIENTS UNDER STANDARD CONDITIONS

In typhoid fever the heat production is increased 30 to 50 per cent., and this makes it difficult to remove all the moisture from the calorimeter, even if the percentage of heat lost in vaporization be not raised. When the patient's temperature begins to fall there is such an increase in water eliminated from the skin that the humidity of the air rises rapidly, often to the point of condensation on the cooling pipes. For

this reason many typhoid experiments are excluded, leaving only those in which the water output was relatively low. If we group those experiments in Table 13 in which the temperature rose 0.3 to 1.0 C., we find the water elimination was decreased to the lower normal limits, 22 per cent. With a temperature that is stationary or changing only 0.2 C. in three hours, the vaporization is about the same as that of normal men, 24 per cent. With a falling temperature there is an increase which may be very marked. After the first week in convalescence the average figure is low, 21 per cent. The findings of Schwenkenbecker[33] are confirmed.

TABLE 14.—Patients with Exophthalmic Goiter

Name	Date	Details Published in Paper	Relative Humidity		H_2O, Gm. per Hour	Per Cent. Calories Lost in Vaporization	Remarks
			Start	End			
Max W.	3/28/14	14	39	48	36	22	Severe hyperthyroidism
	4/ 6/14	14	38	54	35	21	
	4/24/14	14	46	55	37	20	
Edwin T.	3/ 6/15	14	49	42	35	25	Acute, moderately severe
	3/10/15	14	39	40	31	25	
	3/22/15	14	47	51	38	26	
James McE.	3/12/15	14	53	54	43	27	Severe
	3/31/15	14	32	39	32	21	
G. S. L.	4/ 9/14	14	37	43	30	27	Severe
	4/16/14	14	46	53	37	21	
Peter N.	4/14/15	14	35	35	28	22	Atypical
Anna R.	5/10/13	14	44	54	32	30	Moderately severe
	5/14/14	14	40	38	30	25	
Sarah M.	4/29/14	14	52	50	38	30	Mild
Marion B.	2/ 5/15	14	40	47	36	26	Mild
Margaret L.	4/20/14	14	55	54	41	29	Atypical
Bessie H.	4/ 8/14	14	33	35	27	26	Atypical
	4/13/14	14	25	30	21	22	Atypical
	4/18/14	14	32	32	23	26	Atypical

Very recently some experiments have been made on erysipelas patients, using the improved system of ventilation made possible by the new Lehman blower. In one case the body temperature fell 1.2 C. in eight hours, and the percentage of calories lost in vaporization was 27.

33. Schwenkenbecker and Inagaki: Ueber die Schweissekretion im Fieber, Arch. f. exper. Path. u. Pharmakol., 1905, **53**, 365.

In another case the temperature rose 0.8 C. in six hours and 24 per cent. of the calories were used for vaporization.

Exophthalmic Goiter.—In Paper 14 of this series a table was given showing the water elimination of the patients, and the results were briefly discussed. Reviewing the findings critically (Table 14), it is necessary to rule out a large number of experiments in which the water elimination was so great that the ventilating system could not remove the moisture quantitatively. In some of these there may have been no increase in the percentage of heat lost in vaporization. In others there was undoubtedly a rise in water elimination out of proportion to the increase in radiation and conduction. These are the cases which interest us most and it is unfortunate that we cannot determine the water output. Still there remain ten experiments on four men with severe or moderately severe hyperthyroidism in which the technic was satisfactory. Of these, Dr. G. S. L. showed a diminished water elimination, losing only 19 per cent. of his calories in this manner. The other three, Max W., Edwin T., and James McE., were within normal limits in these experiments. We must remember that it was on account of high water elimination that it was necessary to exclude five out of eight observations on Max W., two out of five on Edwin T., and one out of three on James McE. We may conclude that the water elimination in severe hyperthyroidism is usually within normal limits, occasionally decreased, but very often distinctly increased.

TABLE 15.—PERNICIOUS ANEMIA

Name	Date	Details Published in Paper	Relative Humidity		H_2O, Gm. per Hour	Per Cent. Calories Lost in Vaporization	Remarks
			Start	End			
Daniel V.	5/ 9/13	15	49	48	32	27	Hb 25 per cent.
Andrew K.	3/11/14	15	24	32	24	19	Hb 20 per cent.
	3/27/14	15	28	36	29	24	Hb 20 per cent.
Martin C.	5/ 4/15	15	34	32	27	27	Hb 21 per cent.
Bartolo D.	3/15/15	15	19	20	17	19	Hb 44 per cent.
Daniel O'C.	4/26/15	15	30	38	32	30	Hb 40 per cent.

Pernicious Anemia.—Table 15 gives the averages obtained in a series of experiments on patients with pernicious anemia. The average figure, 25 per cent., is almost identical with the standard for normal controls. This shows that the dilution of the blood that is found in severe anemia has no effect on the amount of water vaporized.

TABLE 16.—Cardionephritic Patients

Name	Date	Details Published in Paper	Relative Humidity		H_2O, Gm. per Hour	Per Cent. Calories Lost in Vaporization	Remarks
			Start	End			
Armon W.	2/13/15	16	31	34	28	23	Mitral disease; fibrillation
Fred D.	2/15/15	16	44	45	37	29	Mitral disease; decompensated
	2/23/15	16	34	31	25	26	Mitral disease; compensated
Edward M.	2/17/15	16	44	42	37	25	Mitral disease; fibrillation
Charles L.	2/19/15	16	38	48	37	24	Valvular disease; nephritis
Burel P.	3/24/15	16	40	30	32	23	Valvular disease
August F.	5/ 1/15	16	34	31	26	31	Nephritis; fibrillation
William S.	2/10/15	16	25	29	24	21	Adherent pericardium
George M.	4/ 7/13	16	45	46	24	24	Chronic nephritis
	3/24/14	16	30	32	24	25	
	4/ 4/14	16	27	29	23	23	
David K.	3/21/13	16	55	52	36	24	Chronic nephritis
	3/24/13	16	49	50	28	23	
William A.	1/25/15	16	34	35	33	28	Aortic insufficiency
	1/27/15	16	44	36	32	27	
Theodore S.	1/28/14	16	56	54	39	29	Mitral stenosis; fibrillation
	1/30/14	16	52	56	37	29	
	2/ 9/14	16	31	35	22	24	

Cardionephritic and Nephritic Patients.—The results obtained in a series of patients in which the cardiac element predominated over the nephritic are given in Table 16. It will be seen that the water elimination was increased above the normal in almost all who suffered from moderately severe dyspnea, and in several of those with slight or no dyspnea. We should expect the increased rate of ventilation of the lungs to remove more water by vaporization, but it is quite possible that the skin is also more active. The average for the whole group was 26 per cent.

The results in fourteen experiments on nephritic patients are grouped in Table 17. The average figure, 23 per cent., is only slightly below the standard. It is instructive to group the findings according to the leading symptoms (Table 18).

Since the dyspnea must increase the vaporization from the lungs, we are forced to believe that there is a slight diminution in the water elimination from the skin in severe nephritis. Still we must remember that the total eliminated in vaporization is the same as in the case of a normal man. The waterlogged patient whose kidneys excrete perhaps

TABLE 17.—Fourteen Nephritic Patients

Name	Date	Details Published in Paper	Relative Humidity		H_2O, Gm. per Hour	Per Cent. Calories Lost in Vaporization	Remarks
			Start	End			
Joseph Un.	3/29/16	22	40	43	35	25	Chronic parench. nephritis
	4/ 5/16	22	43	38	28	23	
	4/10/16	22	29	29	22	16	
Lee H.	12/ 4/15	22	27	31	24	27	Chronic parench. nephritis
	1/ 5/16	22	25	30	21	23	
Edna S.	12/ 1/15	22	22	22	18	26	Chronic parench. nephritis
Adam D.	1/14/16	22	26	30	22	22	Chronic parench. nephritis
	2/ 7/16	22	28	30	22	25	
William S.	12/ 6/15	22	30	34	27	21	Chronic parench. nephritis
John K.	3/ 4/16	22	30	33	24	22	Chronic interstitial nephritis
Isadore R.	1/24/16	22	38	42	18	25	Chronic interstitial nephritis; uremia
Frank C.	2/28/16	22	25	34	24	23	Chronic interstitial nephritis; uremia
John C.	2/ 9/16	22	37	37	32	25	Chronic interstitial nephritis
Mildred C.	12/10/15	22	32	34	27	24	Chronic interstitial nephritis

TABLE 18.—Findings in Nephritic Patients Grouped According to Leading Symptoms

Patients with	Percentage of Calories Lost in Vaporization		
	Cardionephritis Group	Nephritic Group	Both Groups
Marked edema	28	24	25
Slight edema	25	22	23
No edema	26	24	24
Marked dyspnea	28	24	26
Slight dyspnea	23	23	25
No dyspnea	26	23	25
Whole group	26	23	24

100 to 400 c.c. a day, eliminates 700 to 800 c.c. water through skin and lungs. It would be interesting to know exactly the effects of hot packs and hot air baths in this disease. Theoretically, we should expect the greatest water vaporization at the highest temperature and the lowest humidity. With increasing humidity the loss from the lungs should decrease and the visible sweat should increase. Rubner and

his associates repeatedly emphasize the depressing effects of moist warm air and the comparative stimulation of dry air.

Diabetes.—In nine out of a total of twenty-nine basal experiments in severe and mild diabetes the percentage of calories lost in vaporization was within normal limits. In ten, the figures were above normal; in nine, below. We must remember that the extremely low metabolism

TABLE 19.—DIABETES

Name	Date	Details Published in Paper	Relative Humidity		H_2O, Gm. per Hour	Per Cent. Calories Lost in Vaporization	Remarks
			Start	End			
Gerald S.	11/ 9/14	17	24	25	21	24	Severe, D:N 1.53
	11/12/14	17	26	28	24	27	Severe, second fast day
	11/14/14	17	20	22	18	23	Severe, fourth fast day; body dried
	11/16/14	17	39	30	28	35	Severe, sixth fast day; body dried
	11/18/14	17	15	17	14	25	Severe, eighth fast day; body dried
	11/23/14	17	15	17	13	21	5th day of feeding; beginning edema
	11/24/14	17	15	17	14	22	6th day of feeding; slight edema
	11/25/14	17	18	18	15	25	7th day of feeding; slight edema
	11/30/14	17	28	25	21	29	Convalescent
	12/ 2/14	17	30	27	24	36	Convalescent
	12/ 4/14	17	22	22	19	24	Convalescent
	12/ 7/14	17	22	22	19	24	Convalescent
William G.	1/11/15	17	21	20	16	22	Sugar-free; emaciated
	1/15/15	17	32	31	24	31	D:N 3.8; emaciated
	1/22/15	17	19	21	18	21	D:N 3.12; emaciated
Joseph U.	2/ 1/15	17	24	21	18	29	Sugar-free; emaciated
Edward M.	10/30/14	17	31	32	26	27	Well nourished
Felix K.	2/11/14	17	33	32	22	20	Sugar-free
	2/26/14	17	25	31	20	16	Sugar-free
	3/20/14	17	22	27	20	19	Sugar-free
Cyril K.	12/16/15	24	34	41	32	23	Severe diabetes; acidosis
	12/18/15	24	43	35	30	23	Severe diabetes; acidosis
	12/20/15	24	24	25	21	18	Severe diabetes; acidosis
	12/22/15	24	27	27	21	19	Severe diabetes; acidosis
	2/16/16	24	17	20	15	17	Recovering
	3/ 8/16	24	27	28	21	29	Recovering
Joseph D.	11/15/15	24	34	35	28	31	Severe diabetes
	11/17/15	24	29	35	24	20	Severe diabetes
	11/19/15	24	46	45	34	36	Severe diabetes
Anna H.	3/31/16	24	27	24	16	32	Much emaciated
Average.....	.....	..	..	..	21	25	

of most of the starved diabetics was accompanied by a very low water output. This in turn made the humidity of the air in the calorimeter much lower than usual, and normal controls, with the relative humidity of 15 to 25 per cent. found in some of the diabetic experiments, might have shown a water elimination somewhat above the standard of 24.1 per cent. obtained when the humidity was 35 to 50 per cent. For this reason the comparison of the starved diabetics with the normals is unsatisfactory. The results in all the experiments are given in Table 19 and the averages for the different phases of the disease are given in Table 20, omitting experiments in which the body temperature changed more than 0.2 C.

TABLE 20.—AVERAGE VAPORIZATION IN DIFFERENT PHASES OF DIABETES

	Number of Observations	Average Percentage of Calories in Vaporization
Severe Diabetes:		
After recent food	1	25
Basal determination	3	24
Second to eighth day of fast	6	25
Sugar-free Fasting	1	26
Basal (emaciated)	8	26
Mild diabetes:		
Well nourished	3	18

The averages in severe diabetes are almost exactly the same as the normal standard, but the variations are large. The amount of water eliminated from the lungs would depend on the rate of ventilation and would be increased in patients with hyperpnea.

SUMMARY AND CONCLUSIONS

The technic of determining the water eliminated from the skin and respiratory passages of a subject in a respiration chamber is exceedingly difficult. If the humidity of the air in the box rises, moisture will be deposited on the contents of the chamber. If the relative humidity falls, water will be removed which was not eliminated by the subject in the experimental period.

Over three hundred experiments have been made in the Sage calorimeter on patients and normal controls at an air temperature of 22 to 25 C. and a relative humidity usually between 30 and 50 per cent. For purposes of comparison all experiments are excluded in which the relative humidity changed more than 10 per cent. between the start and finish of the observation.

TABLE 21.—Water Vaporization of Different Groups of Subjects Studied Under Standard Conditions of Clothing, Temperature and Ventilation. Summary Table

Group of Subjects	Number of Experiments in Group	Percentage of Calories Lost in Vaporization
13 normal men, ages 22 to 44 years	29	24
6 men after glucose or protein	9	23
4 men after 7 to 10 grains of caffein	5	26
8 boys, ages 12 to 13 years	8	27
6 old men, ages 77 to 83 years	6	27
2 legless men	2	25
2 dwarfs (1 rachitic; 1 achondroplastic)	2	23
3 cretinoid dwarfs	4	22
4 typhoid patients, temperature rising 0.3 to 1.0 C.	9	22
5 typhoid patients, temperature change less than 0.3 C. during experiment	6	24
1 typhoid patient, temperature falling 0.4 C.	1	28
3 typhoid patients, 2d to 5th week of convalescence	9	21
5 pernicious anemia patients	6	25
17 cardionephritics and nephritics	24	24
With marked edema	8	25
With slight edema	5	23
With no edema	8	24
With marked dyspnea	6	26
With slight dyspnea	10	23
With no dyspnea	8	25
8 diabetics	30	25

Normal men 20 to 50 years old under the standard conditions excrete on an average 29 gm. water an hour (about 700 gm. a day) through skin and air passages, losing in this manner 24 per cent. of the total heat produced. Few normal men depart more than one-tenth from this figure. All the results on groups of patients are compared with this standard figure of 24 per cent., plus or minus one-tenth. (Table 21.) Boys 12 to 13 years old give figures close to the upper limit and very old men lose almost the same percentage of calories in vaporization. Dwarfs and legless men are also close to the normal average. Cretinoid dwarfs show diminished water elimination. Typhoid patients with a rising temperature also have a decreased water output; those with a falling temperature lose an increased percentage of calories in vaporization. The water output in convalescence is low.

Some patients with hyperthyroidism have a decreased water out-

put; most of them lose the normal percentage of calories in vaporization. Some lose much more than normals in this manner. In pernicious anemia the water of vaporization is not affected. Cardiac and nephritic patients on the whole give figures close to the normal. There is a slight increase in dyspneic patients. Edema seems to have no effect on the water output through the skin. The results in diabetes show great variations. The average figure, however, is about the same as that obtained in normals.

In conclusion it may be said that the output of water is very little affected in disease. When the heat production is increased the body responds and dissipates the usual percentage of calories in the vaporization of water. When it is necessary to get rid of unusual amounts of heat the percentage lost in vaporization is increased.

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